Cule-H02902-10-P024526

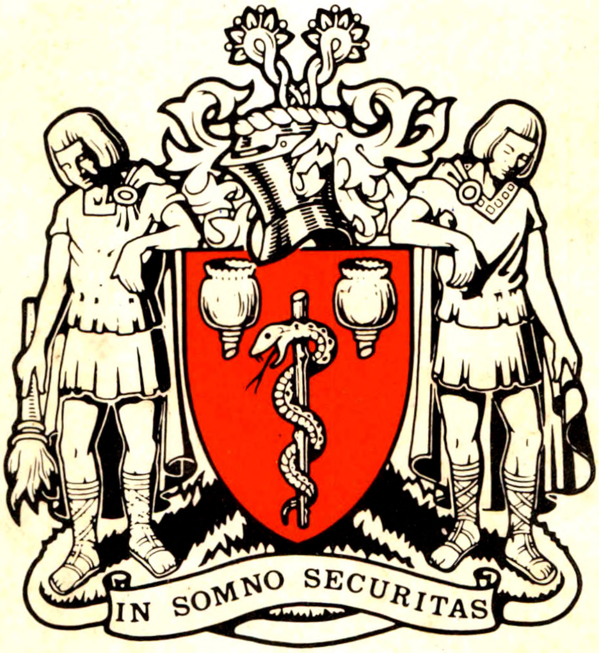
# Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Volume 44 Number 5 May 1989

VOL-44
NO. 5-7
1989

10



The Association of Anaesthetists of Great Britain and Ireland
*Patron*: HRH The Princess Margaret, Countess of Snowdon

Published for the Association by
Academic Press Grune & Stratton
London San Diego New York Boston
Sydney Tokyo Toronto

ISSN 0003-2409

*Some larger species of whale are able to remain submerged for up to an hour before surfacing to breathe. The picture shows a humpback whale (Megaptera novaeangliae).*

At each stage of the operative procedure, 'Diprivan' brings benefits to those concerned.

The anaesthetist achieves smooth induction and well controlled maintenance by repeat bolus or continuous infusion.

Early post-operative assessment by both the surgeon and the anaesthetist is possible, thanks to the patient's rapid recovery.

Above all, the patient quickly regains full mental clarity, usually free from unpleasant after effects, making the task of patient reassurance easier for the nursing staff.

For procedures expected to last up to one hour, 'Diprivan' has made total intravenous anaesthesia a reality.

---

**'DIPRIVAN' ▼ PRESCRIBING NOTES Use** Induction and maintenance of general anaesthesia for surgical procedures lasting up to one hour. **Presentation** Ready to use, isotonic, aqueous emulsion containing 10mg/ml propofol in a vehicle containing soybean oil and purified egg phosphatide. **Dosage and administration Induction** Titrate against response using approximately 4ml every 10 seconds in healthy adults and 2ml every 10 seconds in patients of ASA grades 3 and 4. Patients under 55 years are likely to require 2.0 to 2.5mg/kg, older patients may require approximately 20% less. **Maintenance** Usually 0.1 to 0.2mg/kg/min (6 to 12mg/kg/hr). Continuous infusion may require slightly higher rates for 10 to 20 minutes after induction. Alternatively repeat bolus injections of 25 to 50mg (2.5 to 5.0ml) may be used. **Paediatric Use** No experience in children or in mothers who are breast feeding. **Precautions** Do not mix prior to administration with other agents or infusion fluids. Hypotension and transient apnoea may occur during induction. Occasionally, hypotension may require use of i.v. fluids and lower rate of administration during maintenance. Apply caution in cardiac, respiratory, renal or hepatic impairment; in hypovolaemic or debilitated patients; and in disorders of fat metabolism or conditions where lipid emulsions should be used cautiously. On general principles, do not use in pregnancy except for termination. **Side effects** Bradycardia responsive to atropine has been reported. Epileptiform movements have occurred rarely in temporal relationship to 'Diprivan' but no causal relationship has been established. Nausea, vomiting and headache in a small proportion of patients. Very rarely, a clinical syndrome, which may include bronchospasm and erythema accompanied by hypotension, has been reported with 'Diprivan'. Pain on injection in a proportion of patients. Venous sequelae are rare. Minimal evidence of excitation on induction. **Product licence number** 29/0190 **Basic NHS cost** £3.98 per 20ml ampoule. 'Diprivan' is a trademark. Lower price available for hospitals. Further information is available from: ICI Pharmaceuticals (UK), Southbank, Alderley Park, Macclesfield, Cheshire. SK10 4TF

ICI
*World Class*

**Diprivan**
propofol

VERSATILE MAINTENANCE OF ANAESTHESIA

P, 24,526

# Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editor J. N. LUNN
Associate Editor M. MORGAN
Assistant Editors R. GREENBAUM, R. M. JONES, A. R. AITKENHEAD
Editor of *Anaesthesia News* J. N. HORTON
*Editorial Board*
Chairman The President of the Association M. ROSEN
Members C. F. SCURR, P. J. F. BASKETT, J. EDMONDS-SEAL and a representative of the Junior Anaesthetists' Group
*Ex officio*
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association P. MORRIS
The Assistant Honorary Secretary of the Association W. L. M. BAIRD

*Sub-editors of special sections*
L. KAUFMAN Anaesthetic literature
J. R. DAVIES Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

*Address for literary contributions* Dr J. N. Lunn, The Editor, *Anaesthesia*,
Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff
CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

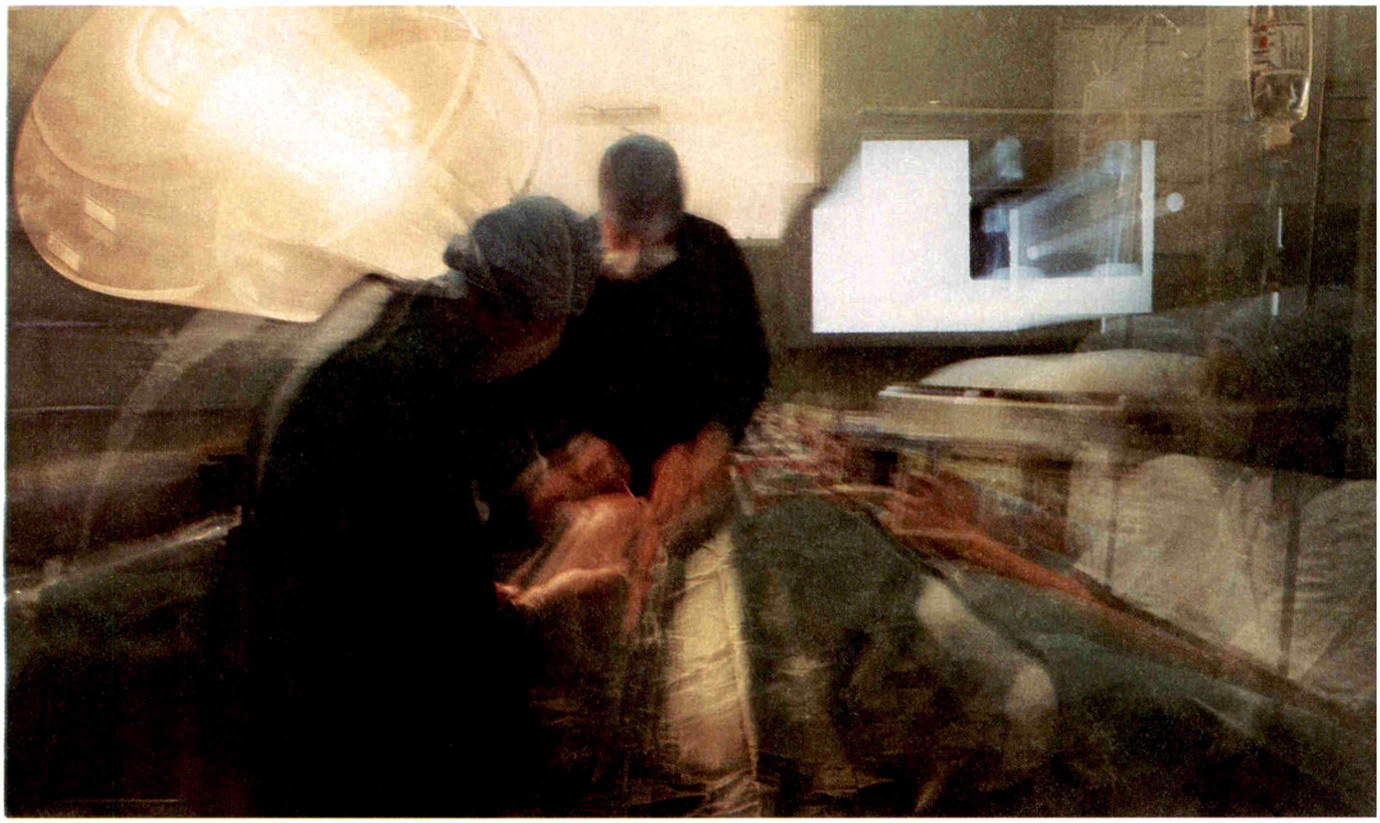
Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. A written statement of this acceptance may be requested by the Editor.

ANAESTHESIA: ISSN 0003-2409. Volume 43 1988, published monthly by Academic Press at 24–28 Oval Road, London NW1 7DX, UK for the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
**All advertising** enquiries should be addressed to the Advertising Department, Anaesthesia, Harcourt Brace Jovanovich, 2nd Floor, 24–28 Oval Road, London NW1 7DX (Tel: 01-267 4466; Telex: 25775 ACPRES G; Fax: 01-482 2293).
Annual subscription price including postage: £98 UK and US $198 overseas. Subscription orders should be sent to Academic Press Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01–300 3322). Send notices of changes of address to the publisher at least 6–8 weeks in advance, including both old and new address.
Second class postage rate paid at Jamaica, NY 11431, USA.
Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
USA POSTMASTERS: send change of addresses to ANAESTHESIA, c/o Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
Printed in UK.

© 1988 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the USA. This consent is given on the condition, within the USA, that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, USA for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the USA.

# Haemaccel®

polygeline



## The flexible solution, with more than a decade of British experience

**Presentation** 500 ml contain 17.5 g polygeline. **Cations:** mmol/500 ml $Na^+$ 72.50 $K^+$ 2.55 $Ca^{++}$ 3.13. **Anions:** mmol/500 ml $Cl^-$ 72.50 $PO_4^{---}$ and $SO_4^{--}$ traces. pH 7.2—7.3. Sterile distilled water to 500 ml. **Uses** As a plasma volume substitute in cases of: **1.** Hypovolaemic shock due to: *a)* Haemorrhage (visible or concealed) *b)* Burns, peritonitis, pancreatitis, crush injuries *c)* Water and electrolyte loss from persistent vomiting and diarrhoea, diseases of the kidneys and adrenals, portal vein thrombosis, ileus, diabetic coma. **2.** Fluid replacement in plasma exchange. **3.** Extra-corporeal circulation. **4.** Isolated organ perfusion. **5.** As a carrier solution for insulin. **Dosage and administration** Haemaccel should be administered intravenously in a volume approximately equal to the estimated blood loss. Normally 500 ml will be infused in not less than 60 minutes, but in emergencies Haemaccel can be rapidly infused. **Hypovolaemic shock** 500-1,000 ml Haemaccel i.v. initially. Up to 1,500 ml blood loss can be replaced entirely by Haemaccel. For between 1,500 ml and 4,000 ml blood loss, fluid replacement should be with equal volumes of Haemaccel and blood, given separately (see Pharmaceutical Precautions). For losses over 4,000 ml the separate infusions should be in the ratio two parts blood to one part Haemaccel. **Burns** At least 1 ml Haemaccel per kg body weight, multiplied by the % of body surface burned should be infused in each 24 hours for two days. **Plasma exchange** Haemaccel should be given either alone or in combination with other replacement fluids in a volume adequate to replace the plasma removed. Up to 2 litres have been given as sole replacement fluid. **Contra-indications, warnings, etc.** There are no absolute contra-indications to the use of Haemaccel. However, caution should be used in any patient likely to develop circulatory overloading. Inappropriately rapid administration of Haemaccel, especially to normovolaemic patients, may cause the release of histamine. In the event of histamine release, the infusion should be discontinued and appropriate action taken with anti-histamines etc. Histamine release may be especially hazardous in patients with known allergic conditions such as asthma. Haemaccel contains calcium ions and caution should be observed in patients being treated with cardiac glycosides. Citrated blood should *not* be mixed with Haemaccel. Haemaccel should, if possible, be warmed to body temperature before use. However, in emergencies it may be infused at ambient temperatures. **Pharmaceutical precautions** As Haemaccel contains no preservatives, any unused fluid should be discarded once a bottle has been opened. Citrated blood may be infused immediately before or after haemaccel provided there is adequate flushing of the infusion set. Date of Preparation: May 1987 Basic Hospital Price: £3.43 per 500 ml bottle PL No.: 0086/0040 Further information available on request. Hoechst U.K. Ltd., Pharmaceutical Division, Hoechst House, Salisbury Road, Hounslow, Middx.

Hoechst UK Limited,
Pharmaceutical Division,
Hoechst House,
Salisbury Road,
Hounslow,
Middlesex TW4 6JH

BEHRING
E v Behring

*Anaesthesia*, 1989, Volume 44, pages 377–378

# Editorial

## Anaesthesia in old age

In the seven ages of man Shakespeare reminds us of the similarities between the young and the old.

> 'Last scene of all,
> That ends this strange eventful history,
> Is second childishness and mere oblivion,
> Sans teeth, sans eyes, sans taste, sans everything.'
> (*As You Like It* 2.7.163)

The old are as different from what may be regarded as physiological normality as are the young. This has crucial consequences with regard to the conduct as well as the risks of anaesthesia and surgery in the old, but much less attention has been paid to this than has occurred at the other extreme of life. There has been less research performed, less written about and less emphasis paid to the specific problems of the old in our anaesthetic training programmes. The on-call junior trainee with a few months' experience, gets on with anaesthetising the old lady with the fractured neck of femur, whilst in the theatre next door, the Consultant and senior trainee anaesthetise the neonate with pyloric stenosis. Yet the expertise and experience required to ensure a successful outcome in the former is at least equal to, and may be more than, that required in the latter. The old are not simply adults with a greater chance of having coexisting disease; they are fundamentally different.

How do they differ? Of particular significance to anaesthetists are changes in general metabolism, cardiorespiratory physiology and the function of the liver and kidney. As a guide, many important physiological functions decrease by about 1% per year after the age of 30. Thus by the age of 70 basal metabolic rate is about 40% of normal and this in itself appreciably delays the excretion and metabolism of anaesthetic drugs. Thermoregulation is impaired, there is osteoporosis, and a loss of muscle tissue with a proportional increase in fatty tissue. Cardiac output reduces by about 1% per year after the age of 30, and circulation time is appreciably prolonged. Diminished arterial elasticity means that systolic hypertension is the rule rather than the exception and autonomic and baroreceptor responsiveness is greatly diminished. The vital capacity, maximal breathing capacity and total lung capacity are all decreased whilst functional residual capacity increases. The arterial $Po_2$ decreases by about 0.07 kPa per year after the age of 20, and at age 70 the normal alveolar-arterial oxygen difference is 2.7 kPa. The ventilatory response to hypercarbia and hypoxia is half that of young persons at age 70 and the laryngeal, pharyngeal and airway reflexes are all less effective. Renal blood flow and glomerular filtration rate decrease by about 1% per year and renal acidification and drug clearance are both reduced. Liver blood flow also decreases by a similar amount and drugs that undergo significant hepatic metabolism will have a longer plasma half-life.

Many factors, some of which have already been noted, are involved in the different sensitivity of the old to drugs in general, and anaesthetic drugs in particular. All anaesthetic drugs are to some extent protein bound and there is a gradual decline in the plasma albumin concentration with age. The effect of this depends on the degree of drug binding to albumin and of course is greater in drugs significantly bound, such as fentanyl (80% binding) than in those less so, such as morphine (40% binding). Barbiturates, narcotics, local anaesthetics and muscle relaxants are all affected. For example, Muravchick and Mandel found that a sleep dose of thiopentone was 1.8 mg/kg in patients aged over 65 years but in 20–40 year olds it was 2.8 mg/kg.[1] Factors other than protein binding are also important and some drugs, because of the multiplicity of factors involved in their kinetics, are handled in a markedly different way by the old. Despite no clinical evidence of hepatic or renal disease, old patients have a five-fold increase in plasma concentration after oral propranolol compared with young patients.[2] The plasma half-life of diazepam increases almost linearly with age[3] and its value in hours is approximately the same as the patient's age in years.

Even in apparently healthy older patients these changes summate to cause an appreciable increase in operative morbidity and mortality. And with advancing age multisystem disease and polypharmacy are the rule rather than exception. The aged have three times the incidence of unwanted drug side effects,[4] are more prone to significant drug interactions and may be taking drugs which are no longer considered first-line therapy (methyldopa or reserpine for hypertension) and with which the younger generation of anaesthetists may be unfamiliar.

The net result is of a substantial risk of anaesthesia and surgery in this age group. Davenport has reported that approximately half of intra-operative deaths occurred in geriatric patients in whom only about 5% of the surgical procedures were performed.[5] In the recently published *Confidential Enquiry into Perioperative Deaths*[6] three-quarters of the patients in the study were over 70 years of age. Emergency surgery in this age group still carries a mortality rate of about 10%.[7] With a growing aged population these considerations and risks become increasingly important. At present about 10% of the population is over 65 years of age, and by the year 2000 this figure will have risen to 12.5%.

Because of the appreciable increase in the risks of anaesthesia and surgery and the prevalence of co-existing disease, the anaesthetist must bring all his physicianship to play when deciding, with the surgeon, about the optimum time for operation. It would be folly to delay surgery unduly just because the values recorded during routine laboratory investigations were suboptimal. Delay of operation for fractured neck of femur, for instance, markedly affects the subsequent independence and morbidity of patients[8] apart from any consideration concerning postoperative mortality.

0003–2409/89/050377 + 02 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

A society may be judged by the quality of care it provides for its more vulnerable members and the elderly must not be forgotten amongst this group.

> 'When thou wast young, thou girdedst thyself, and walkedst whither thou wouldest: but when thou shalt be old, thou shalt stretch forth thy hands, and another shall gird thee, and carry thee whither thou wouldest not.'
>
> (*St. John* 21, 18)

*Guy's Hospital*
*London SE1 9RT*
R.M. JONES

## References

1. MURAVCHICK S, MANDEL J. Thiopental sleep dosages in geriatric patients. *Anesthesiology* 1982; **57:** A327.
2. CASTLEDEN CM, KAYE CM, PARSONS RL. The effect of age on plasma levels of propranolol and practolol in man. *British Journal of Clinical Pharmacology* 1975; **2:** 303–6.
3. MCLESKEY CH. Anesthesia for the geriatric patient. In: STOELTING RK, BARASH PG, GALLAGHER TJ, eds. *Advances in anesthesia, Vol. 2.* Chicago: Year Book Medical, 1985: 31–68.
4. HURWITZ N. Predisposing factors in adverse reactions to drugs. *British Medical Journal* 1969; **1:** 536–9.
5. DAVENPORT HT. Anaesthesia for the geriatric patient. *Canadian Anaesthetists' Society Journal* 1983; **30:** S51–S55.
6. BUCK N, DEVLIN HB, LUNN JN. *Confidential enquiry into perioperative deaths.* London: Nuffield Provincial Hospital Trust, 1987.
7. ZAMOST B, BENUMOF JL. Anesthesia in the geriatric patient. In: KATZ J, BENUMOF JL, KADIS LB, eds. *Anesthesia and uncommon diseases.* Philadelphia: W.B. Saunders, 1981: 98–1180.
8. VILLAR RN, ALLEN SM, BARNES SJ. Hip fractures in healthy patients: operative delay versus prognosis. *British Medical Journal* 1986; **293:** 1203–4.

The group founded to promote research, teaching and training of anaesthesia in older patients is the *Age Anaesthesia Association.* Details of membership may be had from Dr G.A.H. Heaney, Department of Anaesthesia, Good Hope Hospital, Sutton Coldfield, West Midlands B75 7RR.

## Editorial notices

### Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Manuscripts must be submitted in accordance with the internationally recognized *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979; **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

*Anaesthesia*, 1989, Volume 44, pages 379–381

# The effect of acutely administered phenytoin on vecuronium-induced neuromuscular blockade

H. St. J. GRAY, R. M. SLATER, AND B. J. POLLARD

**Summary**

*Phenytoin was administered intravenously in a dose of 10 mg/kg to a group of patients in whom steady state neuromuscular blockade had been established with an infusion of vecuronium. A control group of patients were given 0.9% saline instead of phenytoin. Administration of phenytoin produced significant augmentation of neuromuscular blockade ($p < 0.001$). The possible mechanism of this effect is discussed.*

**Key words**

*Neuromuscular relaxants*; vecuronium.
*Anticonvulsants*; phenytoin.

Sensitivity to certain non-depolarising neuromuscular blocking agents has been demonstrated in patients who receive chronic phenytoin therapy.[1–3] The suggestion was advanced that a pharmacodynamic interaction may be responsible for this effect, in which phenytoin antagonises the action of acetylcholine at the neuromuscular junction.[3] In both *in vitro*, and intact animal models, large doses of phenytoin enhance a non-depolarising neuromuscular blockade induced by tubocurarine.[4] This study was therefore undertaken in order to determine whether the acute administration of a clinically appropriate dose of phenytoin would affect an established non-depolarising neuromuscular blockade induced with vecuronium.

## Methods

Ten patients aged between 24 and 62 years who were scheduled to undergo craniotomy for tumours or cerebrovascular surgery were studied. These patients were considered by the neurosurgeons to require anticonvulsant prophylaxis beginning in the intra-operative period. Patients were not studied if significant renal, cardiovascular, or neuromuscular disease were present, or if they were receiving any drug known to affect neuromuscular transmission. The study protocol was approved by the hospital ethics committee, and informed consent was obtained from each patient.

All patients were premedicated with an oral benzodiazepine given approximately 90 minutes pre-operatively. Surface electrodes were placed over the ulnar nerve at the wrist, and over the ipsilateral *adductor pollicis* muscle before induction of anaesthesia, so that the evoked electromyograph (EMG) could be recorded from the *adductor pollicis* muscle after ulnar nerve stimulation. The stimulation was delivered, and the EMG recorded using a Relaxograph (Datex), which delivers trains-of-four supramaximal stimuli at a rate of 2 Hz, each with a pulse width of 100 μsec every 20 seconds.

Anaesthesia was induced with thiopentone 3–5 mg/kg and fentanyl 3–4 μg/kg administered intravenously. The Relaxograph was then switched on and calibrated. Vecuronium 0.1 mg/kg was given and when adequate muscle relaxation was established, the trachea was intubated and controlled ventilation of the lungs continued.

Anaesthesia was maintained with 70% nitrous oxide in oxygen, to which was added 0.5–1% isoflurane. Routine patient monitoring included continuous ECG display, continuous direct blood pressure recording from a radial artery cannula, end-tidal carbon dioxide concentration, and nasopharyngeal temperature. The patient's temperature was maintained above 36 °C using a warming blanket and condenser humidifier. The end-tidal carbon dioxide concentration was maintained between 3.5% and 4.5% throughout.

An infusion of vecuronium in a concentration of 1 mg/ml was started when the first twitch of the train-of-four (T1) returned. The infusion rate was adjusted to achieve a steady state height of T1 between 5 and 10% of that before

H.St.J. Gray, MRCP, FFARCS, R. M. Slater, MRCP, FFARCS, Senior Registrars, B.J. Pollard, BPharm, FFARCS, Senior Lecturer, Department of Anaesthetics, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL.

Accepted 22 November 1988.

0003–2409/89/050379 + 03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Logarithmic means of T1% over time after phenytoin administration ($n = 10$).

| | Time (minutes) | | | |
|---|---|---|---|---|
| Factor | 0 | 15 | 30 | 45 |
| Mean (SD) | 1.801<br>(0.461) | 1.566<br>(0.748) | 1.375<br>(0.718) | 1.375<br>(0.718) |
| Detransformed means | 6.1 | 4.8 | 4.0 | 4.0 |
| | | NS | $p < 0.001$ | $p < 0.001$ |

**Table 2.** Logarithmic means of T1% over time after 0.9% saline administration ($n = 5$).

| | Time (minutes) | | | |
|---|---|---|---|---|
| Factor | 0 | 15 | 30 | 45 |
| Mean (SD) | 2.004<br>(0.580) | 2.015<br>(0.747) | 2.043<br>(0.723) | 2.046<br>(0.743) |
| Detransformed means | 7.4 | 7.5 | 7.7 | 7.7 |
| | | NS | NS | NS |

neuromuscular blockade, or as near to this range as possible. Phenytoin was administered intravenously in a dose of 10 mg/kg at a rate of 50 mg/minute when neuromuscular blockade had been constant for at least 30 minutes, without any alteration in the infusion rate. The patient's cardiovascular variables were closely monitored and the phenytoin infusion rate reduced if significant hypotension, or changes in the electrocardiogram, occurred. The vecuronium infusion rate and the inhaled concentration of isoflurane were maintained constant during this period.

A second group of five patients was also studied, who were to undergo similar surgical procedures, but did not require anticonvulsant prophylaxis. An identical protocol was followed in this group, except that 20 ml of 0.9% saline was infused instead of phenytoin.

Each patient served as his or her own control; it was possible to compare neuromuscular blockade before and after administration of either phenytoin or saline. The data were found to conform to a log-normal distribution and this transformation was therefore used for analysis. The T1 height before administration of either phenytoin or saline was compared with that at 15, 30, and 45 minutes after the start of the phenytoin or saline infusion, using analysis of variance. Significance was set at the 5% level.

## Results

The steady state neuromuscular blockade in all cases was with T1 between 3 and 13% of control. Table 1 shows the results for those patients who received phenytoin. The T1 height is expressed as percent of the prerelaxant control value. There was a significant increase in neuromuscular blockade at 30 and 45 minutes after the start of the phenytoin infusion. The results for the five patients who received 0.9% saline in place of phenytoin are shown in Table 2. At no time after administration of saline was there a significant change in neuromuscular blockade.

## Discussion

These results indicate that the acute administration of phenytoin enhances a pre-existing vecuronium-induced neuromuscular blockade. This observation concurs with previous animal work which has shown a direct neuromuscular blocking action of phenytoin.[4] There have also been case reports of muscle weakness which has improved after chronic phenytoin therapy was stopped.[5]

The mechanism of action of phenytoin on neuromuscular transmission is complex and has been the subject of extensive research. Reports have shown a postjunctional blocking effect,[5] a prejunctional blocking effect[6] and a reduction in synthesis of acetylcholine.[4] Phenytoin also has a stabilising effect on all neuronal membranes related to its action on transcellular flux of sodium, potassium, and calcium ions.[4,7] It is tempting to attribute the enhanced blockade of neuromuscular transmission seen in our study to a pharmacodynamic interaction, but the possibility of a pharmacokinetic effect cannot be ruled out. Vecuronium is 90% protein bound[8] and phenytoin 80% protein bound.[9] An increased concentration of free active drug after direct displacement of vecuronium from protein binding sites could also offer an explanation for the observations.

In all patients a decrease in systemic arterial blood pressure was observed during the phenytoin infusion, although at no time did the mean arterial pressure fall by more than 20 mmHg. It is possible that a transient reduction of hepatic or renal clearance of vecuronium may have been responsible for the increase in neuromuscular blockade.

The results from the second group of five patients who did not receive phenytoin indicate that the observed effect was not related to slow, continuous accumulation of vecuronium, and that steady-state neuromuscular blockade was actually achieved.

In conclusion, we have demonstrated an additive effect of phenytoin when administered acutely on an established, vecuronium-induced, neuromuscular blockade. The mechanism of this effect cannot be further clarified. The magnitude of this additional neuromuscular blockade when phenytoin is given in a clinically appropriate dose is small, and would be unlikely to be clinically significant.

## Acknowledgment

We thank B. Faragher, Head of the Department of Medical Statistics, Withington Hospital, Manchester, for carrying out the analyses of the data.

## References

1. Ornstein E, Matteo RS, Silverberg PA, Schwartz AE, Young WL, Diaz J. Chronic phenytoin therapy and nondepolarizing muscular blockade. *Anesthesiology* 1985; **63:** A331.
2. Ornstein E, Matteo RS, Young WL, Diaz J. Resistance to metocurine-induced neuromuscular blockade in patients receiving phenytoin. *Anesthesiology* 1985; **63:** 294–8.
3. Ornstein E, Matteo RS, Schwartz AE, Silverberg PA, Young WL, Diaz J. The effect of phenytoin on the magnitude and duration of neuromuscular block following atracurium or vecuronium. *Anesthesiology* 1987, **67:** 191–6.
4. Gandhi IC, Jindal MN, Patel VK. Mechanism of neuromuscular blockade with some antiepileptic drugs. *Arzneimittelforschung* 1976; **26:** 258–61.
5. Norris FH, Colella J, McFarlin D, McFarlin D. Effect of diphenylhydantoin on neuromuscular synapse. *Neurology* 1964; **14:** 869–76.
6. Raines A, Standaert FG. Effects of anticonvulsant drugs on nerve terminals. *Epilepsia* 1969, **10:** 211–27.
7. Yaari Y, Pincus JH, Argov Z. Depression of synaptic

transmission by diphenylhydrantoin. *Annals of Neurology* 1977, **1:** 334–8.

8. FOLDES FF, DEERY A, BENAD G, MCCLOSKEY MA, STRAUCH R. The binding of neuromuscular blocking agents to plasma proteins (abstract). *Anesthesiology* 1982; **57:** A274.
9. GOODMAN LS, GILMAN A. *The pharmacological basis of therapeutics*. Macmillan, 1980: 452–6.

*Anaesthesia*, 1989, Volume 44, pages 382–385

# Haemodynamic responses to nicardipine in humans anaesthetised with halothane

D. C. RAY AND G. B. DRUMMOND

## Summary

*The haemodynamic effects of an infusion of nicardipine were studied noninvasively before, during and after halothane anaesthesia in man, using a simple technique to achieve constant plasma drug concentrations. Eighty patients were randomly allocated to receive an intravenous infusion of either nicardipine or normal saline. Systolic and diastolic arterial pressures were significantly lower and heart rate significantly higher throughout the infusion than before infusion ($p < 0.001$, all variables) in those patients who received nicardipine. The hypotension induced by nicardipine was not affected by induction of anaesthesia; halothane significantly reduced the nicardipine-induced tachycardia ($p < 0.001$). Nicardipine caused no cardiac rhythm disorders. This technique for the intravenous administration of nicardipine achieves appropriate stable plasma concentrations, is devoid of severe haemodynamic disturbance and appears to be safe to use during halothane anaesthesia in patients with normal left ventricular function.*

**Key words**

*Heart*; antiarrhythmics, calcium channel blockers.
*Pharmacology*; nicardipine.

Calcium channel blockers, especially the newer dihydropyridine agents which are structurally related to nifedipine, represent an interesting group of drugs for the treatment of hypertension, myocardial ischaemia, and cerebral and coronary vasospasm during anaesthesia.[1] Few of these agents, unfortunately, exist in a stable intravenous formulation. Nicardipine hydrochloride is, however, both water soluble and photoresistant and can be given intravenously but as an infusion only, because bolus injection is relatively ineffective.[2]

Significant haemodynamic alterations can occur in conscious subjects in association with infusions of nicardipine;[3,4] although it was administered as bolus injections in conjunction with anaesthesia,[5,6] there is little information on the haemodynamic consequences of nicardipine infusion during anaesthesia. Nicardipine pharmacokinetics are altered in dogs anaesthetised with isoflurane[7,8] but there is no equivalent information relevant to man.

We intended to assess the influence of nicardipine on the effects of halothane on liver function, the results of which are published elsewhere.[9] We were able to assess in addition the haemodynamic effects of nicardipine infusion at stable plasma concentrations and evaluate possible pharmacodynamic interactions between nicardipine and halothane. We also hoped to examine whether nicardipine steady-state plasma concentrations changed when halothane anaesthesia was induced.

## Materials and methods

### *Patient selection*

The study was approved by the area ethics committee and respected the Declaration of Helsinki. Eighty patients aged 18–70 years old, of ASA class 1 or 2 who were to have minor orthopaedic surgery such as arthroscopy, gave consent to be studied. Obesity (weight > 120% expected), excessive alcohol intake (> 3 units/day) or a past history of liver disease resulted in exclusion. No patient included in the study was receiving regular oral medication of any sort. All were normotensive, in normal sinus rhythm, and were allocated according to a previously prepared, sex-stratified randomised list, to receive either an intravenous infusion of nicardipine or a comparable infusion of normal saline.

### *Infusion plan*

The infusion was designed to achieve a stable plasma nicardipine concentration of about 120 ng/ml after one hour of infusion, based on an estimated plasma clearance

---

D.C. Ray, MB, ChB, Research Fellow, G.B. Drummond, MB, ChB, FFARCS, Consultant, University Department of Anaesthetics, The Royal Infirmary, Lauriston Place, Edinburgh EH3 9YW.
Accepted 27 October 1988.

0003–2409/89/050382 + 04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

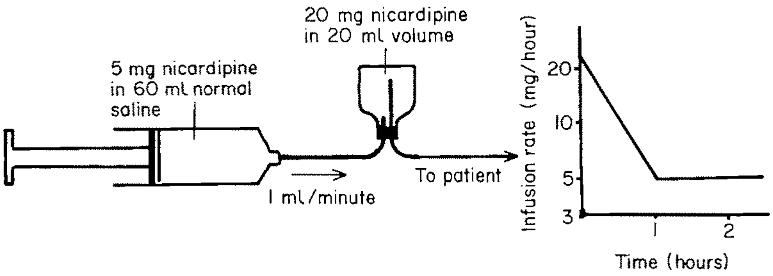


**Fig. 1.** Schematic representation of solution delivery in exponentially decreasing concentration.

rate of nicardipine of 600 ml/minute for an adult subject and an elimination rate constant[10] of 0.2/hour. The contents of a syringe which contained 5 mg nicardipine in 60 ml normal saline were infused from a syringe pump at a rate of 1 ml/minute into a closed vial that contained nicardipine 20 mg in 20 ml volume. The infusion was led from this vial to the patient, a technique similar to that described by Riddell and coworkers,[11] and illustrated schematically in Figure 1. A patient allocated to have nicardipine would have received, in the first hour of this treatment, a combination of a steady infusion of nicardipine 5 mg and an exponentially decreasing infusion with a total of nicardipine 20 mg, that would have been about 95% completely administered in that time. Subsequently a constant infusion of nicardipine in normal saline (0.5 mg/ml) was given for a further 5 hours at a rate of 5 mg/hour.

The infusion was started one hour before induction of anaesthesia. The electrocardiograph was monitored continuously and arterial blood pressure was measured non-invasively and automatically at 5-minute intervals (15-minute intervals in the postoperative period) for the duration of the infusion. The infusion was stopped if the systolic blood pressure became less than 75% of the pre-infusion value, or if tachycardia > 150 beats per minute, or disorders of cardiac rhythm became apparent.

Blood sampling for nicardipine assay was performed after one hour of infusion (i.e. at the end of the exponential infusion) and at 30 minutes, 1, 2, 3 and 6 hours after induction of anaesthesia.

### *Anaesthetic technique*

Premedication was with oral temazepam 2 hours before operation. Anaesthesia was induced with intravenous thiopentone 4–6 mg/kg and was maintained with 66% nitrous oxide, 1.5–2% (inspired) halothane and balance oxygen. All patients breathed spontaneously through a circle system with a carbon dioxide absorber. Duration of anaesthesia was restricted to 30–90 minutes.

### *Assay procedures*

Samples for nicardipine assay were separated by centrifugation and the resultant serum was stored at −20°C until assay was performed by the standard high performance liquid chromatography method.[12]

### *Statistical analysis*

The systolic arterial pressures (SAP), diastolic arterial pressures (DAP) and heart rates for each group were analysed at the following seven times: before infusion, 5, 10 and 60 minutes after the infusion was started, 15 minutes after the induction of anaesthesia, at the end of anaesthesia, and at the conclusion of the infusion. The demographic data, SAP, DAP and heart rate in the two groups were compared with Student's *t*-test.

## Results

Eighty patients entered the study: 42 received nicardipine (27 males, 15 females) and 38 placebo (26 males, 12 females). Patients in the two groups were comparable in age, height, weight and % expected weight (Table 1). The infusion was discontinued in 11 patients, eight of whom had received nicardipine and on each occasion the infusion was stopped because of hypotension (Table 2). No patient who had nicardipine exhibited tachycardia > 150 beats/minute, or cardiac arrhythmia which necessitated discontinuation of the infusion. Three patients who received normal saline also had the infusion stopped; two because of tachycardia and one whose operation was cancelled. Nicardipine plasma concentrations are shown in Table 3. The 6-hour sample was taken after the infusion was completed and explains the apparent discrepancy in nicardipine concentration at that time.

Mean values for SAP, DAP and heart rate at each time of analysis, for both the nicardipine and placebo groups, are shown in Figure 2. Results from the two groups show that SAP was significantly lower in the nicardipine group only at 10 minutes after the start of the infusion. This compares with DAP which was significantly lower and heart rate significantly higher in patients who received nicardipine at all times of analysis after the start of the infusion, except at the end of anaesthesia. The tachycardia induced by nicardipine was significantly reduced during anaesthesia, in relation to values before and after operation ($p < 0.001$).

## Discussion

The administration technique we describe resulted in plasma nicardipine levels compatible with those which give clinically apparent effects in previous work.[3] Steady-state plasma levels were achieved after one hour of infusion, whereas in earlier work in which an initial exponential infusion was not administered, the time taken to achieve steady-state was about 140 minutes.[13] This method of administration appears to achieve steady-state conditions reliably and rapidly and maintain appropriate plasma concentrations without causing severe haemodynamic disturbance.

**Table 1.** Demographic data for patients who had nicardipine infusion and placebo. Values expressed as mean (SD).

| | Placebo | Nicardipine |
|---|---|---|
| Age, years | 34 (11) | 32 (10) |
| Height, cm | 173 (9) | 175 (10) |
| Weight, kg | 72 (11) | 74 (13) |
| % expected weight | 102 (12) | 104 (12) |

**Table 2.** Details of the discontinued nicardipine infusions.

| Duration infusion (minutes) | % decrease in systolic arterial pressure | Systolic arterial pressure (mmHg) | Nicardipine concentration (ng/ml) |
|---|---|---|---|
| 15 | 36 | 90 | — |
| 105 | 27 | 93 | 143.6 |
| 115 | 35 | 89 | 57.1 |
| 95 | 28 | 98 | 85.2 |
| 103 | 25 | 96 | 84.8 |
| 138 | 30 | 89 | 62.1 |
| 95 | 27 | 86 | 144.5 |
| 188 | 39 | 75 | 133.2 |

**Table 3.** Medians of nicardipine plasma concentrations expressed as HCl equivalent in ng/ml (interquartile range).

| End of exponential infusion | Hours | | | | |
|---|---|---|---|---|---|
| | 0.5 | 1 | 2 | 3 | 6 |
| 125.3<br>(102.1–149.5) | 97.1<br>(85.2–115.9) | 98.5<br>(84.9–109.0) | 87.5<br>(76.9–105.4) | 97.6<br>(76.8–106.3) | 35.2<br>(28.3–42.7) |

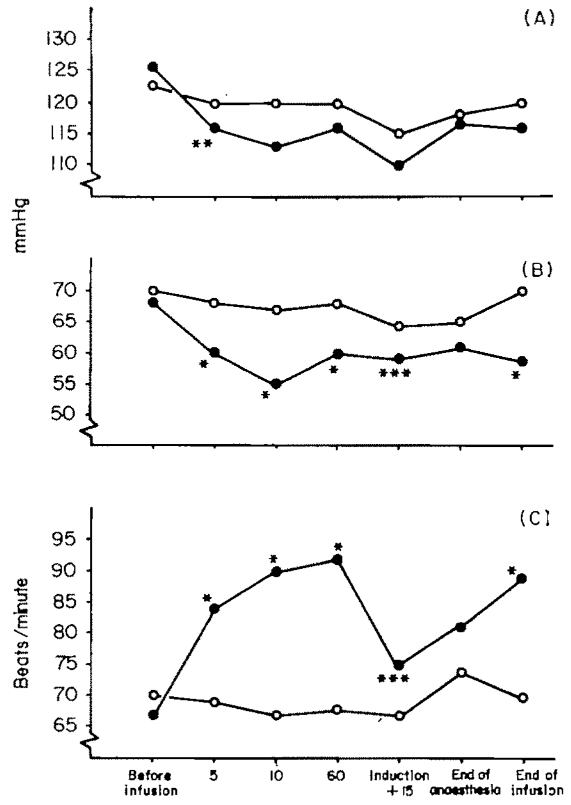


Fig. 2. Graphs of systolic arterial pressure (A), diastolic arterial pressure (B) and heart rate (C) of patients who received nicardipine and saline infusions, showing differences between the groups at each time of analysis. ○——○, placebo; ●——●, nicardipine. *, $p < 0.001$; **, $p < 0.01$; ***, $p < 0.05$.

Reports exist of patients who receive calcium channel blockers and suffer from haemodynamic disturbances under anaesthesia.[14–16] Merin has reviewed the interaction between these drugs and anaesthetics in relation to benefit or detriment.[17] Five of the eight discontinued nicardipine infusions were stopped during anaesthesia when the combination of halothane and nicardipine would be expected to cause most hypotension. Thus only three of the 42 patients who received nicardipine had the infusion stopped solely because of the influence of the infusion itself. Eight of the nicardipine infusions were stopped because SAP decreased to less than 75% of the control value, but in only one patient was the actual level of SAP below 85 mmHg at the time of stopping. Such levels of SAP may be seen during halothane anaesthesia alone and thus the level of hypotension experienced by those patients who had the infusion discontinued would not be considered to be particularly severe. We have demonstrated that nicardipine infusion caused a significant increase in heart rate within minutes of commencing the infusion. This was sustained throughout the duration of the infusion and did not cause disorders of cardiac rhythm.

The hypotension induced by nicardipine was not affected by induction of anaesthesia. Subjects who received a placebo exhibited in contrast a significant reduction in arterial pressure during anaesthesia compared with the awake state. Since nicardipine lowers blood pressure by peripheral arterial vasodilatation and the blood pressure decrease which accompanies halothane anaesthesia is primarily due to reduced myocardial contractility, this suggests that the hypotensive properties of nicardipine and halothane could be additive or synergistic. Similar interactions have been reported between nicardipine and isoflurane[18] and nifedipine and halothane.[19–20]

Halothane blunted the tachycardia associated with nicardipine infusion and this confirms previous observations.[18,19] This is also supported by the work of Kishi and others[5] who reported no increase in heart rate on bolus injection of nicardipine to patients anaesthetised with high-dose fentanyl. The increase in heart rate associated with nicardipine is probably a reflex baroreceptor-mediated response to reduced arterial pressure. Halothane inhibits the baroreflex pathway[21] thus this inhibition of baroreceptor reflex function may play an important role in the reduction of nicardipine-induced tachycardia under halothane anaesthesia. This halothane-induced reduction in heart rate reduces myocardial oxygen demand, which could be beneficial especially in patients with ischaemic heart disease.

We detected, apart from this reduction of tachycardia, no other pharmacodynamic interaction of consequence between nicardipine and halothane in the present study; the two agents seem safe to administer together in patients with normal left ventricular function. The effect of concurrent administration of these two drugs to a patient with poor left ventricular function has yet to be assessed.

Only verapamil, and much more recently nimodipine, exist in a commercially available intravenous preparation. Nifedipine and nitrendipine exist for intravenous administration only in a formulation for investigation, but both compounds are unstable when exposed to light. Intravenous nicardipine is photoresistant.

The effects of verapamil administration during halothane anaesthesia are reported[15] and it appears that these two agents may be used together. However, a major problem of verapamil administration during halothane anaesthesia is the potential development of atrioventricular block[22] which may be difficult to reverse.[23] The main indication for intravenous nimodipine (which is slowly deactivated on exposure to light) is in the acute management of cerebral vasospasm, especially after subarachnoid haemorrhage, where it increases cerebral perfusion with minimal effect on systemic blood pressure and heart rate.[24] Nicardipine has been administered intravenously during anaesthesia with isoflurane,[18] fentanyl[5,6] and now halothane (present study) with no untoward effects.

Isoflurane has been reported to have profound effects on the pharmacokinetics of nicardipine in dogs.[7,8] Volume of distribution and clearance were both significantly reduced, but since both were reduced comparably elimination half-life was unaffected. In the present study halothane did not appear to alter the steady-state plasma concentration of nicardipine. Little more can be inferred from our data about the effect of halothane on the pharmacokinetics of nicardipine, because to ensure a bloodless operating field the majority of patients had a pneumatic tourniquet applied to the appropriate limb for the course of the operation, and this might have influenced pharmacokinetic parameters.

We have described a technique for the intravenous administration of nicardipine which achieves appropriate steady-state blood levels, is devoid of gross haemodynamic disturbance and is safe when administered concurrently with halothane.

## Acknowledgments

This work was supported by Syntex Pharmaceuticals Ltd., and was performed while D.C.R. held a Syntex research fellowship in the Department of Anaesthetics, University of Edinburgh. We are grateful for the assistance from the anaesthetic, surgical, nursing and theatre staff at the Princess Margaret Rose Orthopaedic Hospital, without whose help the study could not have been performed.

## References

1. Reves JG, Kissin I, Lell WA, Tosone S. Calcium entry blockers: uses and implications for anesthesiologists. *Anesthesiology* 1982; **57:** 504–18.
2. Campbell BC, Kelman AW, Hillis WS. Noninvasive assessment of the haemodynamic effects of nicardipine in normotensive subjects. *British Journal of Clinical Pharmacology* 1985; **20:** 55–61S.
3. Debbas NMG, Jackson SHD, Turner P. A study of the haemodynamic effects of nicardipine infusion in man. *British Journal of Clinical Pharmacology* 1985; **19:** 563–4P.
4. Jamieson MJ, Jeffers TA, Dow R, Graham D. Nicardipine infusion: pharmacokinetics, haemodynamics and effects on the systolic time intervals. *British Journal of Clinical Pharmacology* 1985; **19:** 536P.
5. Kishi Y, Okumura F, Furuya H. Haemodynamic effects of nicardipine hydrochloride. Studies during its use to control acute hypertension in anaesthetized patients. *British Journal of Anaesthesia* 1984; **56:** 1003–6.
6. Begon C, Dartayet B, Edouard A, David D, Samii K. Intravenous nicardipine for treatment of intraoperative hypertension. *Anesthesiology* 1987; **67:** A39.
7. Merin RG, Chelly JE, Hysing ES, Abernethy DR, Doursout M-F, Jacobson L, Kiechel JR. Effect of isoflurane (Iso) on nicardipine (Nc) pharmacokinetics. *Clinical Pharmacology and Therapeutics* 1986; **39:** 210.
8. Chelly JE, Hysing ES, Merin RG, Abernethy DR, Doursout M-F, Hartley CJ, Guerret M. Role of anesthesia (A) on nicardipine (Nc) plasma concentration(PC)-effect relationship. *Clinical Pharmacology and Therapeutics* 1986; **39:** 186.
9. Ray, DC, Beckett GJ, Hayes JD, Drummond GB. The effect of nicardipine infusion on the release of glutathione S-transferase following halothane anaesthesia. *British Journal of Anaesthesia* (in press).
10. Graham DJM, Dow RJ, Hall DJ, Alexander OF, Mroszczak EJ, Freedman D. The metabolism and pharmacokinetics of nicardipine hydrochloride in man. *British Journal of Clinical Pharmacology* 1985; **20:** 23–85.
11. Riddell JG, McAllister CB, Wilkinson GR, Wood AJJ, Roden DM. A new method for constant plasma drug concentrations: application to lidocaine. *Annals of Internal Medicine* 1984; **100:** 25–8.
12. Wu AT, Massey IJ, Kushinsky S. A high-performance liquid chromatographic method for the simultaneous determination of nicardipine and its pyridine metabolite II in plasma. *Journal of Pharmaceutical Sciences* 1984; **73:** 1444–7.
13. Graham DJM, Dow RJ, Freedman D, Mroszczak E, Ling T. Pharmacokinetics of nicardipine following oral and intravenous administration in man. *Postgraduate Medical Journal* 1984; **60** (Suppl. 4): 7–10.
14. Prys-Roberts C. Anaesthesia and hypertension. *British Journal of Anaesthesia* 1984; **56:** 711–24.
15. Brichard G, Zimmermann PE. Verapamil in cardiac dysrhythmias during anaesthesia. *British Journal of Anaesthesia* 1970; **42:** 1005–12.
16. Gorven AM, Cooper GM, Prys-Roberts C. Haemodynamic disturbances during anaesthesia in a patient receiving calcium channel blockers. *British Journal of Anaesthesia* 1986; **58:** 357–60.
17. Merin RG. Calcium channel blocking drugs and anesthetics: is the drug interaction beneficial or detrimental? *Anesthesiology* 1987; **66:** 111–13.
18. Hysing ES, Chelly JE, Doursout M-F, Hartley C, Merin RG. Cardiovascular effects of and interaction between calcium blocking drugs and anesthetics in chronically instrumented dogs. III. Nicardipine and isoflurane. *Anesthesiology* 1986; **65:** 385–91.
19. Tosone SR, Reves JG, Kissin I, Smith LR, Fournier SE. Hemodynamic responses to nifedipine in dogs anesthetized with halothane. *Anesthesia and Analgesia* 1983; **62:** 903–8.
20. Kates RA, Zaggy AP, Norfleet EA, Heath KR. Comparative cardiovascular effects of verapamil, nifedipine and diltiazem during halothane anesthesia in swine. *Anesthesiology* 1984; **61:** 10–18.
21. Seagard JL, Hopp FA, Donegan JH, Kalbfleisch JH, Kampine JP. Halothane and the carotid sinus reflex: evidence for multiple sites of action. *Anesthesiology* 1982; **57:** 191–202.
22. Kapur PA, Flacke WE. Epinephrine-induced arrhythmias and cardiovascular function after verapamil during halothane anesthesia in the dog. *Anesthesiology* 1981; **55:** 218–25.
23. Jones RM. Calcium antagonists. *Anaesthesia* 1984; **39:** 747–9.
24. Tettenborn D, Dycka J, Volberg E, Dudden P. Blood pressure and heart rate during treatment with nimodipine in patients with subarachnoid hemorrhage. *Neurochirurgica* 1985; **28** (Suppl. 1): 84–6.

*Anaesthesia*, 1989, Volume 44, pages 386–388

# The effects of speed of injection on induction with propofol

## A comparison with etomidate

G. W. A. GILLIES AND N. W. LEES

## Summary

*One hundred and eighty female patients received either propofol 2.5 mg/kg or etomidate 0.3 mg/kg injected over 20, 40 or 80 seconds for induction of anaesthesia after premedication with temazepam 20 mg. The mean induction times for both etomidate and propofol were significantly reduced with increasing speed of injection. The mean induction times for etomidate were significantly less than propofol at the slower rates of injection. At each speed of injection, the decrease in systolic, mean and diastolic arterial blood pressures with etomidate were less than with propofol. The decrease in systolic blood pressure was not significantly affected by injection speed for either drug. Apnoea occurred significantly more frequently with propofol than with etomidate at each speed of injection and the incidence of apnoea greater than 60 seconds with propofol was significantly higher when injected over 20 seconds than 80 seconds. The incidence of pain on injection was unaffected by injection speed for either drug. The incidence of myoclonus and (or) hypertonus was significantly higher following etomidate.*

**Key words**

*Anaesthetics, intravenous*; etomidate, propofol.

Propofol is an intravenous induction agent which combines the desirable characteristics of smooth induction and rapid recovery from anaesthesia.[1,2] It has, however, been shown to cause a marked decrease in arterial blood pressure[3,4] and its use has been associated with a high incidence of pain on injection.[2,3] Etomidate causes little cardiovascular depression[5] but carries a high incidence of involuntary movements and pain on injection.[6]

The purpose of this study was to determine the effects of different speeds of injection on the induction characteristics of propofol and etomidate.

## Methods

The study was approved by the hospital ethics committee and all patients gave informed consent. One hundred and eighty female patients aged 16–60 years, scheduled to undergo minor gynaecological surgery, were entered in the study. All patients were ASA grade 1 or 2. They were allocated randomly to one of six groups to receive either propofol, 2.5 mg/kg, or etomidate, 0.3 mg/kg, administered over 20, 40 or 80 seconds. All patients received a premedication of temazepam 20 mg orally approximately one hour pre-operatively.

A 20-gauge cannula was inserted into a vein in the dorsum of the hand and a Dinamap automatic blood pressure cuff was attached to the opposite arm before induction. To provide an end point for induction of anaesthesia, the patients were asked to hold the tip of a water-filled 20-ml syringe between their thumb and index finger as described by Cummings *et al.*[7] The induction agent was then injected over the specified duration. The patient was asked if her hand was comfortable when about half the drug was administered. Pain on injection was noted if the patient either complained of pain spontaneously or in response to this question. Complaints of cold or other sensations were not included.

A mask was applied to the patient's face and she breathed 33% oxygen in nitrous oxide from a Magill system after induction. Two minutes after the start of injection, enflurane was introduced for maintenance of anaesthesia.

The following observations were made: time to induction, presence of pain on injection, hypertonus, myoclonus and spontaneous movements. Cardiovascular indices of pulse rate, systolic, diastolic and mean arterial blood pressure were recorded immediately before induction and at 2 minutes after the start of injection. Observations were also made of any respiratory effects such as cough, hiccough, laryngospasm and incidence and duration of apnoea, which was defined as the absence of spontaneous ventilation for 15 seconds or more. Apnoea lasting more

---

G.W.A. Gillies,* FFARCS, Senior Registrar, N.W. Lees, FFARCS, Consultant, Department of Anaesthetics, Victoria Infirmary, Glasgow G42 9TY.

*Present address: Consultant, Department of Anaesthetics, Victoria Infirmary, Glasgow G42 9TY.

Accepted 18 October 1988.

0003–2409/89/050386 + 03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Demographic data of patients. Values expressed as mean (SD).

| | Etomidate 20 seconds | Etomidate 40 seconds | Etomidate 80 seconds | Propofol 20 seconds | Propofol 40 seconds | Propofol 80 seconds |
|---|---|---|---|---|---|---|
| Patients ($n$) | 30 | 30 | 30 | 30 | 30 | 30 |
| Age, years | 32.8 (10.7) | 33.7 (11.8) | 38.2 (11.6) | 32.4 (11.3) | 32.0 (12.6) | 37.8 (11.9) |
| Weight, kg | 61.9 (9.3) | 60.0 (9.4) | 58.9 (7.9) | 61.9 (8.1) | 58.9 (8.9) | 59.2 (8.4) |
| Height, cm | 162.3 (7.1) | 161.5 (5.5) | 159.1 (5.8) | 161.2 (6.1) | 162.7 (6.8) | 161.4 (6.6) |

**Table 2.** Induction times. Values expressed as mean (SD).

| | Etomidate | Propofol |
|---|---|---|
| Time, seconds | | |
| 20 | 32.0 (4.4) | 30.8 (4.3) |
| 40 | 38.6 (6.1) | 43.7 (7.8) |
| 80 | 50.9 (11.1) | 58.4 (11.4) |

than 60 seconds was considered prolonged and manual ventilation of the lungs was instituted until spontaneous breathing resumed.

An assessment of the overall quality of induction was also made, taking into account side effects which were considered to affect adversely the smooth onset of induction. All observations were made by the same investigator.

Statistical analysis was carried out using Student's $t$-test for demographic data; a two-tailed Mann–Whitney $U$ test for induction times and cardiovascular data. A Chi-squared test with Yates' correction was used for other data.

## Results

The ages, weights and heights of the patients are shown in Table 1. No significant differences were found within the etomidate or propofol groups or between groups at the same speed of injection. All of the patients were successfully anaesthetised except one in the etomidate 40-second group who received a supplement of etomidate 4 mg after 90 seconds because of marked spontaneous movement of both arms.

The induction times are shown in Table 2. For both etomidate and propofol the induction times of the 20-second groups were significantly shorter than the 40-second groups ($p < 0.001$) which in turn were significantly shorter than the 80-second groups ($p < 0.001$). In addition, the induction times for the etomidate 40- and 80-second groups were significantly shorter compared with the corresponding propofol groups ($p < 0.001$).

The changes in systolic, mean and diastolic arterial pressures and pulse rate from pre-induction levels to the values at 2 minutes after the start of injection are shown in Table 3. Data from two patients in the etomidate 40-second group were not included, in one because the patient had been given a supplementary dose of etomidate and in the other because the data were not recorded. Altering the speed of injection had no significant effect on the change in systolic, mean or diastolic pressures with etomidate. The change in systolic arterial pressure for patients who received propofol was not significantly affected by alteration in speed of injection. Significantly greater decreases in both mean and diastolic pressures with propofol were found in the 80-second group compared with the 40-second group ($p < 0.001$).

The decrease in systolic, diastolic and mean arterial pressures with etomidate were significantly less than with propofol ($p < 0.001$) at each speed of injection. The fall in blood pressure for any individual patient was never sufficient to cause concern.

Alteration of speed of injection had no effect on pulse rate with propofol. The group which received etomidate over 80 seconds had a significantly reduced fall in pulse rate compared with the groups that received etomidate over 20 ($p < 0.05$) and 40 seconds ($p < 0.001$). The pulse rate tended to fall with etomidate but remained unchanged or increased slightly with propofol.

The incidence of side effects is shown in Table 4. The speed of injection significantly influenced the incidence of apnoea with propofol but not with etomidate. Patients who received propofol over 80 seconds had a significantly lower incidence of prolonged apnoeas ($n = 3$) compared with those who received the drug over 20 seconds ($n = 12$, $p < 0.01$). Apnoea occurred significantly more frequently with propofol than etomidate for each injection time ($p < 0.001$ for the 20- and 80-second groups; $p < 0.01$ for the 40-second group). Prolonged apnoea also occurred significantly more frequently with propofol than etomidate when injected over 20 seconds ($p < 0.001$) and 40 seconds ($p < 0.05$).

The incidence of pain on injection overall was higher with etomidate but no clear effect of speed of injection was evident. No patients developed laryngospasm. The incidence of hypertonus and (or) myoclonus was significantly higher with etomidate than propofol at each speed of injection ($p < 0.01$ for 20 and 40 seconds; $p < 0.001$ for 80 seconds). They also occurred significantly more frequently when etomidate was injected over 80 seconds compared with 20 seconds ($p < 0.05$). The incidence of phlebitis or late discomfort that affected veins was not recorded because many patients returned home the same day.

The results of the assessment of quality of induction are shown in Table 5. Ninety-two percent of patients who

**Table 3.** Change in systolic, mean and diastolic arterial pressure and pulse rate from pre-induction to value at 2 minutes. Values expressed as mean (SD).

| | Etomidate 20 seconds | Etomidate 40 seconds | Etomidate 80 seconds | Propofol 20 seconds | Propofol 40 seconds | Propofol 80 seconds |
|---|---|---|---|---|---|---|
| Systolic blood pressure, mmHg | −7.6 (14.8) | −5.4 (17.7) | −2.4 (14.2) | −21.0 (17.4) | −19.0 (16.3) | −25.3 (14.8) |
| Mean blood pressure, mmHg | −0.9 (11.3) | 0.3 (17.6) | 1.6 (11.9) | −16.1 (12.4) | −12.3 (12.9) | −22.1 (14.7) |
| Diastolic blood pressure, mmHg | −1.6 (10.2) | −2.1 (15.0) | −0.7 (8.9) | −14.0 (11.3) | −11.6 (10.7) | −18.4 (9.9) |
| Pulse rate, beats/minute | −9.7 (23.8) | −10.4 (12.6) | −1.9 (8.4) | −1.0 (18.5) | 2.1 (13.7) | 3.2 (11.5) |

**Table 4.** Incidence of side effects.

| | *n* | Apnoea ⩾ 15 seconds | Apnoea ⩾ 60 seconds | Pain | Cough/ hiccough | Hypertonus/ myoclonus | Spontaneous movement | Flush/ rash |
|---|---|---|---|---|---|---|---|---|
| Etomidate 20 seconds | 30 | 4 | 1 | 24 | 6 | 13 | 2 | 0 |
| Etomidate 40 seconds | 30 | 4 | 1 | 14 | 5 | 14 | 1 | 0 |
| Etomidate 80 seconds | 30 | 0 | 0 | 18 | 1 | 21 | 2 | 1 |
| Propofol 20 seconds | 30 | 21 | 12 | 13 | 1 | 4 | 1 | 2 |
| Propofol 40 seconds | 30 | 14 | 6 | 14 | 1 | 4 | 4 | 0 |
| Propofol 80 seconds | 30 | 14 | 3 | 13 | 0 | 5 | 2 | 2 |

**Table 5.** Assessment of quality of induction.

| | Good | Adequate | Poor |
|---|---|---|---|
| Etomidate 20 seconds | 16 | 12 | 2 |
| Etomidate 40 seconds | 18 | 9 | 3 |
| Etomidate 80 seconds | 20 | 8 | 2 |
| Propofol 20 seconds | 18 | 10 | 2 |
| Propofol 40 seconds | 21 | 9 | 0 |
| Propofol 80 seconds | 23 | 7 | 0 |

received etomidate were considered to have an adequate or better quality of induction; this compares with 98% with propofol. This appeared to be uninfluenced by the speed of injection.

## Discussion

To determine an end point for induction with propofol is less easy than with other induction agents because some patients continue to have active eyelash reflexes when anaesthesia appears otherwise to have been satisfactorily induced. The authors found the syringe-holding method described by Cummings *et al.*[7] most useful. The most marked effect of altering the speed of injection was on induction times. Faster speeds of injection reduced the time to induction for both propofol and etomidate. The induction times with etomidate were less than with propofol at the slower injection rates.

The marked difference in effects on arterial blood pressure between etomidate and propofol has also been reported by McCollum and Dundee.[4] The lack of effect of speed of injection on the change in systolic and diastolic blood pressures with etomidate found in this study was also noted by Lees and Hendry.[8] Rolly[9] found no significant effect of speed of injection on the decrease in blood pressure with propofol, which was confirmed in the present study with respect to systolic pressures. The finding that propofol injected over 80 seconds produced a greater decrease in diastolic and mean blood pressures than when injected over 40 seconds was unexpected. We found no difference between the values at 20 and 80 seconds.

Apnoea occurred more frequently with propofol than etomidate. This difference may be partly explained by the finding by Choi *et al.*[10] that etomidate produces a $CO_2$-independent stimulation of ventilation. No significant effect of speed of injection on apnoea was found with etomidate, although no episodes of apnoea occurred with the slowest speed of injection. In contrast, there was a higher incidence of prolonged apnoea with propofol injected over 20 seconds than 80 seconds. Used clinically, a slower injection rate may well result in some patients receiving a reduced dose (mean time to induction was 58 seconds for the 80-second group) and this would also tend to reduce the incidence of apnoea. This suggests a benefit for a slower injection rate with this drug.

The incidence of pain on injection was high for both drugs although greater with etomidate (62%) than propofol (44%). We found no effect of speed of injection on incidence of pain with either drug. Our overall incidence of pain on injection with propofol was much higher than the 5% reported by Rolly[9] who injected into a forearm vein with a fast running dextrose infusion, but similar to the 38% described by Fahy *et al.*[3] who used a needle in the dorsum of the hand.

The incidence of myoclonus and/or hypertonus was markedly greater with etomidate than propofol. The incidence with etomidate was significantly higher when injected over 80 seconds than 20 seconds. These figures include myoclonus of a minor degree that affected face or fingers only. The quality of induction was independent of speed of injection for both drugs.

In conclusion, both drugs produced a satisfactory quality of induction in over 90% of cases. Speed of injection has little effect on induction characteristics with either drug, but there may be some benefit in a slower speed of injection with propofol to reduce the incidence of prolonged apnoea.

## References

1. MacKenzie N, Grant IS. Comparison of the new emulsion formulation of propofol with methohexitone and thiopentone for induction of anaesthesia in day cases. *British Journal of Anaesthesia* 1985; **57**: 725–31.
2. O'Toole DP, Milligan KR, Howe JP, McCollum JSC, Dundee JW. A comparison of propofol and methohexitone as induction agents for day case isoflurane anaesthesia. *Anaesthesia* 1987; **42**: 373–6.
3. Fahy LT, van Mourik GA, Utting JE. A comparison of the induction characteristics of thiopentone and propofol (2,6-di-isopropyl phenol). *Anaesthesia* 1985; **40**: 939–44.
4. McCollum JSC, Dundee JW. Comparison of induction characteristics of four intravenous anaesthetic agents. *Anaesthesia* 1986; **41**: 995–1000.
5. Criado A, Maseda J, Navarro E, Escarpa A, Avello F. Induction of anaesthesia with etomidate: haemodynamic study of 36 patients. *British Journal of Anaesthesia* 1980; **52**: 803–5.
6. Zacharias M, Clarke RSJ, Dundee JW, Johnston SB. Evaluation of three preparations of etomidate. *British Journal of Anaesthesia* 1978; **50**: 925–9.
7. Cummings GC, Dixon J, Kay NH, Windsor JPW, Major E, Morgan M, Sear JW, Spence AA, Stephenson DK. Dose requirements of ICI 35,868 (propofol, 'Diprivan') in a new formulation for induction of anaesthesia. *Anaesthesia* 1984; **39**: 1168–71.
8. Lees NW, Hendry JGB. Etomidate in urological outpatient anaesthesia. A clinical evaluation. *Anaesthesia* 1977; **32**: 592–602.
9. Rolly G, Versichelen L, Huyghe I, Mungroop H. Effect of speed of injection on induction of anaesthesia using propofol. *British Journal of Anaesthesia* 1985; **57**: 743–6.
10. Choi SD, Spaulding BC, Gross JB, Apfelbaum JL. Comparison of the ventilatory effects of etomidate and methohexital. *Anesthesiology* 1985; **62**: 442–7.

*Anaesthesia*, 1989, Volume 44, pages 389–391

# Bed rest and postlumbar puncture headache

## The effectiveness of 24 hours' recumbency in reducing the incidence of postlumbar puncture headache

P. T. COOK, M. J. DAVIES AND R. E. BEAVIS

### Summary

*A prospective, blind, randomised trial was undertaken to determine if the incidence of postlumbar puncture headache is significantly altered by 24 hours' recumbency. One hundred and two patients were allocated randomly to rest supine in bed for either 4 or 24 hours after spinal anaesthesia for urological or gynaecological surgery. A standardised spinal anaesthetic technique was applied that incorporated the use of a 22-gauge needle. All patients were followed-up prospectively to determine if there was a difference in the incidence of postlumbar puncture headache between the two groups. Five patients (11.6%) who were recumbent for 4 hours developed postlumbar puncture headache, a result which was not statistically significantly different from the seven patients (11.9%) in the other group who complained of postlumbar puncture headache.*

**Key words**

*Anaesthetic techniques, regional*; spinal.
*Complications*; headache.

The reported incidence of headache after lumbar puncture varies between 0.4%[1] and 70%.[2] The postlumbar puncture headache is thought to result from leakage of cerebrospinal fluid (CSF) through the dural puncture site into the epidural and paravertebral spaces. The resultant low CSF pressure causes gravity-dependent traction on pain-sensitive structures within the cranial cavity. Posture-dependent headache may result and if severe may be accompanied by nausea and vomiting. Use of fine needles is usually accompanied by a lower incidence of these headaches.[3] Postlumbar puncture headaches also appear to be more common in younger patients,[4] especially those under the age of 60 years. Perhaps in older patients a greater degree of tamponade is produced by the leaked CSF because escape from the epidural space through the intervertebral foramina may be reduced in older patients. An alternative explanation of the lower incidence in older patients is that the greater degree of cerebral vascular atherosclerosis found in the elderly may prevent stretching of their cerebral vessels in the face of low CSF pressure.

It has been common practice to insist on 24 hours' bed rest after dural puncture in patients who undergo spinal anaesthesia. The rationale for this practice was to allow the dural hole to repair itself, at least to some extent, before ambulation. A recent study of patients who underwent dural puncture with 18-gauge needles in the course of neurological investigation has cast doubt on the effectiveness of this practice.[5] No well controlled prospective trial has been performed in surgical patients to validate these results, and so a randomised prospective trial was conducted in surgical patients to assess the influence of 24 hours' recumbency on the incidence of lumbar puncture headache and to compare this with patients who have only 4 hours' recumbency.

### Methods

The sample population consisted of patients presenting for potentially minor urological or gynaecological surgery, but whose medical condition warranted spinal anaesthesia in the opinion of the attending anaesthetist. Only patients who were able to be mobilised within 4 hours of surgery were entered into the trial. The spinal anaesthetics were performed in a standardised fashion. The midlumbar vertebrae were identified and a 22-gauge spinal needle was inserted after infiltration of the skin and subcutaneous tissues with lignocaine. The needle bevel was inserted parallel to the dural fibres. Patients who had one dural puncture performed were included in the study. Lignocaine 5%, 1.5 ml in 6% dextrose, was injected with confirmatory aspirations of small amounts of CSF half way through and at the completion of the injection. The patients were immediately placed supine and taken to the operating theatre.

---

P.T. Cook, FFARACS, R.E. Beavis, FFARACS, Staff Anaesthetists, M.J. Davies, FFARACS, Director, Department of Anaesthesia, St. Vincent's Hospital, Victoria Parade, Melbourne, Victoria, 3065, Australia.
Correspondence should be addressed to Dr M.J. Davies please.

Accepted 18 October 1988.

0003–2409/89/050389 + 03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Intravenous fluids were administered according to a strict protocol. Compound sodium lactate 5 ml/kg was given before arrival in the operating theatre and a further 1.25 ml/kg before arrival in the recovery room. Postoperatively the infusion was changed to 5% dextrose and 500 ml given over 4 hours, after which the intravenous fluids were stopped and normal diet restarted. Patients were allocated randomly after operation to either the 4-hour (Group 1) or 24-hour (Group 2) recumbency groups. Appropriate instructions to nursing staff were recorded in the postoperative orders.

Patient follow-up was achieved either by patients returning a questionnaire through the post, or more commonly by direct telephone interview on the fourth day after operation. The telephone interviewer was unaware of the length of the patient's postoperative recumbency.

No indication was given to the patient at interview of the nature of the investigation. They were asked a series of general questions about what they could remember on the day of surgery and if they had suffered from any of four specific postoperative complaints: cough, dizziness, headache or backache. No particular emphasis was placed on any one of these symptoms. No indication was given to the patient that a headache was a well recognised complication of spinal anaesthesia. The patients were asked to grade subjectively any complaint as mild, moderate or severe and if any complaint was posture dependent (i.e. worse on standing).

Statistical analyses using Student's *t*-test, Chi-squared test and Fischer's exact test were used where appropriate and $p < 0.05$ was taken as a significant difference.

## Results

One hundred and twenty-nine patients were entered into the trial and nine of these were lost to follow-up. A further 18 patients were involved in breaches of the study protocol; this usually involved mobilising later than the 4 hours stipulated in Group 1. Of the remaining 102 patients, 59 were mobilised at 24 hours (Group 2) and 43 at 4 hours (Group 1). There was no statistically significant difference between the groups in terms of age or sex (Table 1). Twelve patients (11.8%) complained of postoperative headache which was worse on standing (Fig. 1). There was no statistically significant difference in the incidence of postlumbar puncture headache between the two groups.

Seven patients complained of severe postlumbar puncture headache; patient discomfort was judged to be sufficiently severe to warrant epidural blood patch in three of them; of these, one was in Group 1 and the other two in Group 2. All headaches had occurred by the end of the second postoperative day (Table 2). The mean age of the 12 patients who developed headache (58.5 years) and of the 90 who did not (65.0 years) did not differ significantly. (Difference = 6.5 years, standard error of the difference = 4.2, $t = 1.54$, degrees of freedom = 100, $p > 0.05$, 95% confidence interval = 0.5 to +13.5).

A total of 31 patients complained of postoperative back pain (Table 3). The length of postoperative recumbency did not affect the incidence of back pain. However, there was a significantly higher incidence of back pain in younger patients (mean age of those with back pain 58.8 years, those without 66.6 years, difference = 7.8 years, standard error of the difference = 2.9, $t = 2.7$, degrees of freedom = 100, $p < 0.01$, 95% confidence interval = 4.8 to 10.8).

**Table 1.** Details of patients. Group 1, 4 hours' recumbency, Group 2, 24 hours' recumbency.

| | Group 1 | Group 2 | Difference |
|---|---|---|---|
| Number of patients | 43 | 59 | NS |
| Age, mean (SD) | 63 (13) | 65 (14) | NS |
| Gender, Male | 30 | 44 | NS |
| Female | 13 | 15 | NS |
| Patients who developed postlumbar puncture headache | 5 (11.6%) | 7 (11.9%) | NS |

NS, not significant.

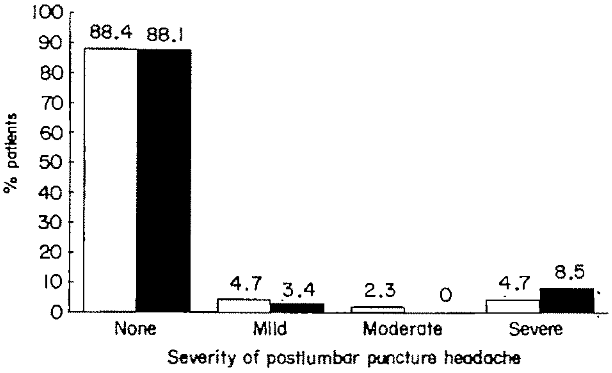


**Fig. 1.** Percentage of patients with no, mild, moderate, or severe postlumbar puncture headache. □, 4 hours' rest in bed ($n = 43$); ■, 24 hours' rest in bed ($n = 59$).

**Table 2.** Day of onset of postlumbar puncture headache. Group 1, 4 hours' rest in bed, Group 2, 24 hours' rest in bed.

| | Day of operation | Day 1 | Day 2 |
|---|---|---|---|
| Group 1 | 2 | 2 | 1 |
| Group 2 | 1 | 6 | 0 |

**Table 3.** Incidence of backache after spinal anaesthesia. Group 1, 4 hours' rest in bed, Group 2, 24 hours' rest in bed.

| | Group 1 | Group 2 | Difference |
|---|---|---|---|
| Back pain | 12 | 19 | NS |
| No back pain | 31 | 40 | NS |

NS, not significant.

## Discussion

Headache is a difficult entity to investigate clinically. Not only is it a subjective phenomenon and therefore not easy to quantify, but it is also a complaint of some patients in the postoperative period even if lumbar puncture has not been performed. Many studies on this subject fail to identify clearly the criteria used to diagnose a headache as a result of lumbar puncture. In this study the authors considered all headaches which were worse on standing and relieved by adopting the supine posture as caused by lumbar puncture. This criterion resulted in classification of postlumbar puncture headache in 12 of the studied patients. However, only seven of these were classed as severe by the patients (6.9%). This is still a high incidence of postoperative morbidity.

A review of the literature on the subject of headache after lumbar puncture reveals a wide variation in the reported incidence. Undoubtedly this variation is at least partly because of the vigour with which a complaint of headache is sought from the patients. Studies which rely on patients who spontaneously report headache almost certainly significantly underestimate the true incidence. However, it is equally important that the study design does not overly suggest headache as a sequela of the procedure. In this investigation, because both treatment regimens are well accepted clinical practice, our patients were neither told the exact purpose of the study nor that the incidence of headache was being specifically studied. The authors tried at the postoperative interview to ascertain if headache was present, without emphasising it as an expected postoperative symptom. The power of suggestion in the causation of headache was demonstrated by Kaplan[6] who, in a study of 100 subjects, showed that there was no statistically significant difference in the incidence of postlumbar puncture headache between a group given a genuine lumbar puncture and a group who underwent a sham lumbar puncture.

The wealth of contradictory clinical investigation on the subject is reflected in contemporary literature. For instance, a recent letter[7] suggested that the incidence of postlumbar puncture headache could be reduced from 13% to 0.4% by a change in needle size from 25 to 26 gauge, in fact a remarkably unlikely occurrence. This literature reflects the various methods which have been popular to reduce the incidence of postlumbar headache. Thus Brocker[8] claimed that a prone posture for 3 hours after lumbar puncture was associated with an incidence of headache of 0.5% with an 18-gauge needle compared to 36.5% in a group kept supine. The fact that this technique is not in widespread use today was explained by a more recent study,[9] also using 18-gauge needles, which found a headache incidence of 33% at one week in a group similarly kept prone for 4 hours immediately after lumbar puncture.

It is still common for anaesthetists to insist on 24 hours' bed rest after lumbar puncture although the efficacy of this practice in preventing headache was questioned by a study in patients who underwent diagnostic lumbar puncture with 18-gauge needles in the course of neurological investigation.[5] No significant difference was found in the incidence of headache between a group ambulant immediately after lumbar puncture (38%) compared with a group confined to bed for 24 hours (36%). Unfortunately patients were not randomly allocated to the two treatment groups.

It is obviously not possible to mobilise all surgical patients immediately after lumbar puncture. We have found, however, that if lignocaine 5% heavy is used as the local anaesthetic agent, mobilisation is possible at 4 hours. This should be done cautiously in elderly patients, because sympathetic blockade can occasionally persist for a surprisingly long time. Our patients are asked to sit up and if after a few minutes no dizziness or significant hypotension is evident they are helped to stand.

Thirty percent of the patients in this study complained of backache in the postoperative period and this was more common in young patients. Whether this backache was due to the local trauma caused during a lumbar puncture or because of the resultant muscular laxity in the lumbar spine is uncertain. All of our patients were placed in the lithotomy position intra-operatively which may have contributed to backache. Flaatten and Raeder[10] in a study of 51 male patients (mean age 38 years) who had spinal anaesthesia with 25-gauge needles found a 55% incidence of backache. Thus it would appear that backache is more common after spinal anaesthesia than is widely appreciated. Twenty-four hours' enforced recumbency did not reduce the incidence of backache in this study.

We conclude that there is no statistical difference in the development of postlumbar puncture headache when recumbency is 4 or 24 hours and it is now our policy to mobilise patients after spinal anaesthesia at 4 hours after surgery as long as there is no surgical or anaesthetic contraindication.

## References

1. Greene BA. A twenty-six gauge lumbar puncture needle: its value in the prophylaxis of headache following spinal analgesia for vaginal delivery. *Anesthesiology* 1950; **11:** 464–9.
2. Crawford JS. Experience with epidural blood patch. *Anaesthesia* 1980; **35:** 513–5.
3. Tourtellotte WW, Henderson WG, Tucker RP, Gilland O, Walker JE, Kokman E. A randomized, double-blind clinical trial comparing the 22 versus 26 gauge needle in the production of the post-lumbar puncture syndrome in normal individuals. *Headache* 1972; **12:** 73–8.
4. Bridenbaugh PD, Greene NM. Spinal (subarachnoid) neural blockade. In: Cousins MJ, Bridenbaugh PO, eds. *Neural blockade in clinical anaesthesia and management of pain.* Philadelphia: J.B. Lippincott, 1988: 246.
5. Carbaat PAT, Van Crevel H. Lumbar puncture headache: controlled study on the preventive effect of 24 hours' bed rest. *Lancet* 1981; **2:** 1133–5.
6. Kaplan G. The psychogenic etiology of headache post lumbar puncture. *Psychosomatic Medicine* 1967; **29:** 376–9.
7. Edmondson L, Erwin DC. (Letter) Spinal anaesthesia in pregnant patients. *Anaesthesia* 1987; **42:** 666–7.
8. Brocker RJ. Technique to avoid spinal-tap headache. *Journal of the American Medical Association* 1958; **168:** 261–3.
9. Handler CE, Perkin GD, Smith FR, Rose FC. Posture and lumbar puncture headache: a controlled trial in 50 patients. *Journal of the Royal Society of Medicine* 1982; **75:** 404–7.
10. Flaatten H, Raeder J. Spinal anaesthesia for outpatient surgery. *Anaesthesia* 1985; **40:** 1108–11.

*Anaesthesia*, 1989, Volume 44, pages 392–393

# Gelling of urea-linked gelatin with fresh frozen plasma

F. MURRAY AND P. HUTTON

**Summary**

*Urea-linked gelatin and succinylated gelatin were mixed with fresh frozen plasma and human albumin solutions in vitro, in varying concentrations and at different temperatures. Gelling was only seen in those mixtures that contained fresh frozen plasma and urea-linked gelatin. It occurred at both room temperature and 37°C when the mixture contained more than 40% by volume of urea-linked gelatin. Further tests confirmed that this was the result of calcium ions in the urea-linked gelatin allowing coagulation to occur in the fresh frozen plasma.*

**Key words**

*Blood*; volume, plasma expanders.
*Veins*; complications.

Twice during separate liver transplantations, when one of the intravenous fluid administration sets was fully opened after being switched off for approximately 20 minutes, there was no flow despite the use of a pressure infusor. On both occasions, when the Luer lock connexion between the warming coil and the infusion set was disconnected, a plug of white gelatinous material was found to occupy the lumen of the two tubes. The plug was found to be 450 mm long when one of the warming coils was sectioned. Both infusion systems had been used earlier for the administration of urea-linked gelatin, succinylated gelatin, clear fluids, 4.5% human albumin solution and fresh frozen plasma. The product information supplied with these solutions does not refer to any potential hazards which might result from their sequential administration.

This study was undertaken because of the practical importance of such reactions, firstly to identify those conditions and combinations of solutions which could result in gel formation and secondly to try to define the causative mechanism.

## Methods

Three groups of experiments were performed

### Group 1

Freshly prepared Group 0 negative cryoprecipitate poor fresh frozen plasma (FFP) and 4.5% human albumin solution (HA) were each separately mixed with both urea-linked gelatin (Haemaccel) and succinylated gelatin (Gelofusin). Solutions were prepared containing concentrations of FFP and HA that ranged from 10% by volume to 90% by volume in increments of 10%. The mixtures, together with samples of each individual solution, were then incubated in clear glass test tubes at 20°C and 37°C for up to one hour. Each test tube was inspected at intervals of 5 minutes to detect any gelling. The degree of gelling was noted and categorised as absent, slight, moderate or extreme. Gelling was said to be slight if strands of gel were visible within the liquid, moderate if most of the solution became gelled with some liquid remaining and extreme if the whole solution became a solid gelatinous mass.

### Group 2

A solution of 0.9% saline was prepared which contained calcium chloride in a concentration of 6.25 mmol/litre. This solution was then mixed with varying volumes of FFP in a manner similar to that described in the Group 1 experiments. Incubation at 37°C followed and observations were made every 5 minutes for one hour. Details of any gelling which occurred were recorded.

### Group 3

The standard anticoagulant solution used by the Blood Transfusion Service [63 ml of citrate phosphate dextrose adenine formula 1 anticoagulant solution, (Fenwal, Travenol)], was diluted to 500 ml with 0.9% saline and 2.5

---

F. Murray, FFARCS, Registrar, Central Birmingham Health District, Birmingham, P. Hutton, PhD, FFARCS, Professor, University of Birmingham, Birmingham B15 2TH.

Accepted 8 November 1988.

0003–2409/89/050392 + 02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** The gelling pattern resulting from mixing urea-linked gelatin and fresh frozen plasma at 37°C.

| Urea-linked gelatin (%) | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| Fresh frozen plasma (%) | 10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 | 90 |
| *minutes* | | | | | | | | | |
| 5 | — | — | — | — | — | — | — | — | — |
| 10 | M | M | M | M | S | — | — | — | — |
| 15 | E | E | E | E | M | S | — | — | — |
| 20 | E | E | E | E | E | M | — | — | — |
| 25 | E | E | E | E | E | E | — | — | — |
| 30 | E | E | E | E | E | E | — | — | — |
| 35 | E | E | E | E | E | E | — | — | — |
| 40 | E | E | E | E | E | E | — | — | — |
| 45 | E | E | E | E | E | E | — | — | — |
| 50 | E | E | E | E | E | E | — | — | — |
| 55 | E | E | E | E | E | E | — | — | — |
| 60 | E | E | E | E | E | E | — | — | — |

S, slight gelling; M, moderate gelling; E, extreme gelling; —, gelling absent.

mmol/litre of calcium chloride. The resulting solution was then mixed with varying volumes of urea-linked gelatin in a manner similar to that described in the Group 1 experiments. Incubation at 37°C followed and observations were made every 5 minutes for one hour. Details of any gelling which occurred were recorded.

## Results

In the Group 1 experiments gelling only occurred in those solutions which contained a mixture of urea-linked gelatin and FFP, and when the percentage of the gelatin component was 40% or greater. The detailed gelling pattern of the solutions at 37°C is shown in Table 1. The gelling pattern at 20°C was virtually identical except that no gelling was observed until 15 minutes had elapsed.

In the Group 2 experiments, gelling occurred after 10 minutes in those solutions in which the calcium containing component was 70% or greater by volume. It was also present after 15 minutes in the solution in which the calcium containing component was 60%. No other gelling was seen up to one hour.

In the Group 3 experiments, no gelling of any degree was ever observed.

## Discussion

The properties of gelatins have recently been reviewed comprehensively[1] and the authors commented on the dangers of mixing urea-linked preparations with citrated blood. We are unaware of any literature which warns of reactions between gelatins and FFP and it was not uncommon practice in our hospital to follow the one with the other. It can be seen from the results of our Group 1 experiments that there is a concentration and time dependent reaction which occurs when FFP is mixed with urea-linked gelatin, (Table 1) but not when it is mixed with succinylated gelatin.

There are two possible mechanisms for this reaction. Firstly, the free calcium ions in the urea-linked gelatin (6.25 mmol/litre) could overwhelm the chelating properties of the citrate that remained in the FFP and allow the FFP to coagulate, or secondly the absorption of calcium by the citrate could adversely affect the ionic stability of the gelatin solution.[2] The Group 2 and Group 3 experiments were set up to clarify this problem. In the Group 2 experiments, the concentration of calcium ions was made identical to that found in commercially available urea-linked gelatin (Haemaccel). The anticoagulant solution in the Group 3 experiments was diluted to be the equivalent of the average volume of blood drawn from an individual donor and the calcium added was the equivalent of that in normal human serum. It is clear from a comparison of the results of the Group 2 and Group 3 experiments that the anticoagulant solution has no effect on the ionic stability of the urea-linked gelatin (Group 3 results), but that the calcium in the urea-linked gelatin is sufficient under certain conditions to exceed the chelating capacity of the anticoagulant solution (Group 2 results). Our results show that when urea-linked gelatin was present in a quantity of 40% or over by volume that the chelating capacity of the citrate in the FFP used was exceeded.

It is quite possible that anaesthetists have administered urea-linked gelatin and FFP sequentially on many occasions without observing any problems, because it is only under certain conditions of concentration and time that gelling occurs. It should perhaps be noted that because of variations in donor blood volume and haematocrit, not all FFP solutions contain exactly the same concentration of anticoagulant solution and that citrate is also present in variable quantities in SAG-M blood.

It is obviously important not to allow FFP and urea-linked gelatin to mix, if they are to be used sequentially. This is however not always easy to achieve since axial streaming can occur,[3] and many times the volume of the tube may be required for adequate flushing. If the latter is incomplete, axial streaming produces a long interface for any potentially reactive constituents to be brought into contact. This effect probably explains the presence of the 450-mm length of clot in the patient described here.

The present work has demonstrated that it is potentially hazardous to infuse sequentially urea-linked gelatin and FFP and that gelling occurs as a result of the free calcium ions in the gelatin component overwhelming the chelating capacity of the citrate in the FFP. It would therefore seem sensible to use succinylated gelatin in those patients in whom there is a possibility that FFP may have to be given through the same intravenous administration set.

## References

1. Saddler JM, Horsey PJ. The new generation gelatins. *Anaesthesia* 1987; **42:** 998–1004.
2. Garside JE, Phillips RF. *A text book of pure and applied chemistry*. London: Pitman Medical, 1965: 338–47.
3. Hutton P, Thornberry EA. Drug delivery via extension tubing. *British Journal of Anaesthesia* 1986; **58:** 1141–8.

*Anaesthesia*, 1989, Volume 44, pages 394–397

# Effect of buprenorphine on the cardiovascular response to tracheal intubation

F. A. KHAN AND R. S. KAMAL

## Summary

*The effects of buprenorphine on the haemodynamic responses to tracheal intubation were studied in a placebo-controlled double-blind trial in 40 patients who had elective surgery. In one group saline was administered intravenously 8 minutes before induction, whereas the others received buprenorphine 2.5 μg/kg intravenously. Anaesthesia was induced in both groups with thiopentone 4 mg/kg followed by suxamethonium 1.5 mg/kg after 90 seconds. In the buprenorphine group, the maximum increase in systolic and diastolic arterial blood pressures, heart rate and rate pressure product were significantly lower compared to the control group. It is concluded that buprenorphine is partially effective in attenuating the cardiovascular response to laryngoscopy and intubation, but does not obliterate it.*

## Key words

*Analgesics, narcotic*; buprenorphine.
*Intubation, tracheal*; complications.

The hypertension and tachycardia in response to laryngoscopy and intubation under a standard thiopentone–suxamethonium technique is a sympathetic reflex provoked by the stimulation of epipharynx and larynx.[1] Other contributory causes can be anxiety, hypercarbia and hypoxaemia, atropine premedication and a reflex baroreceptor effect as a result of the decrease in arterial pressure after thiopentone.[2] The transient rise in systolic arterial blood pressure is approximately 20–25 mmHg and peaks approximately 30–45 seconds after laryngoscopy.[3] Recent work has shown that significant increases in blood pressure occur after laryngoscopy with or without tracheal intubation,[4] but the latter was associated with a significant increase in heart rate.

These haemodynamic changes are serious enough in normotensive individuals, but are of greater significance in patients with coronary artery disease and cerebrovascular disorders,[5] and have been recognised as a potential source of a number of complications.[6–10] Various attempts have been made to attenuate these responses, but none has achieved widespread acceptance. Deep inhalational anaesthesia, systemic and topical lignocaine,[11–13] antihypertensive drugs,[14] beta adrenoceptor blockers[15] and peripheral vasodilators[16,17] have all been used and recommended. Intravenous narcotics have been tried with variable degrees of success.[18–21]

Buprenorphine is a mixed agonist–antagonist narcotic which may have certain advantages in anaesthetic practice.[22,23] The object of our study was to see if buprenorphine, given intravenously before rapid sequence induction, can reduce the increase in systolic and diastolic arterial pressures, heart rate and rate pressure product. This induction sequence was chosen because it is commonly used in everyday clinical practice.

## Methods

Forty adult ASA 1 and 2 male and female patients aged between 18 and 60 years who had elective surgical procedures that required tracheal intubation were entered in the trial. Patients with a past or present history of hypertension were not studied. The patients were premedicated with oral diazepam 0.15 mg/kg 2 hours before surgery; no anticholinergic was used. Patients were randomly allocated to one of two groups. Systolic arterial pressure, diastolic arterial pressure, mean arterial pressure and heart rate were recorded on arrival in the operating room after a stabilisation period of 5 minutes. Any patients with a resting blood pressure above 150/90 mmHg took no further part in the study. The blood pressure was assessed with an Omega 1400 noninvasive blood pressure monitor. The $CM_5$ lead was continuously monitored to detect any myocardial ischaemia.[24]

Group 1 subjects received a saline placebo approximately

---

F.A. Khan, FFARCS, Assistant Professor, R.S. Kamal, FFARCS, Associate Professor, Department of Anaesthesiology, The Aga Khan University Hospital and Medical College, Stadium Road, P.O. Box 3500, Karachi 74800, Pakistan.
Accepted 24 October 1988.

0003–2409/89/050394 + 04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Pre-operative data. Values are expressed as mean (SEM).

| Group | *n* | Age (years) | Weight (kg) | Resting heart rate (beats/minute) | Resting blood pressure (mmHg) Systolic | Diastolic | Mean |
|---|---|---|---|---|---|---|---|
| Control | 20 | 39.6<br>(2.12) | 60.3<br>(2.41) | 85.5<br>(3.63) | 136.7<br>(4.36) | 81.7<br>(2.73) | 96.6<br>(6.3) |
| Buprenorphine | 20 | 36.7<br>(1.40) | 64.7<br>(2.25) | 84.0<br>(2.79) | 136.6<br>(4.21) | 84.6<br>(1.82) | 98.8<br>(3.3) |
| p values | >0.5 | >0.1 | >0.1 | >0.5 | >0.5 | >0.1 | >0.5 |

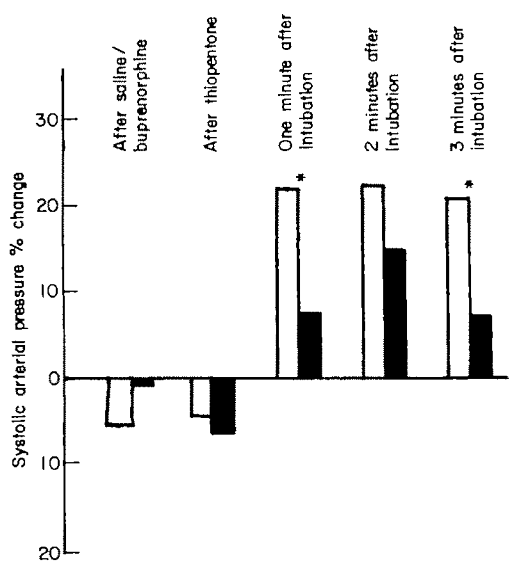


**Fig. 1.** Systolic blood pressure changes compared to baseline values expressed in percentage, in saline and buprenorphine groups following thiopentone, 1, 2, and 3 minutes after intubation □, Group 1, saline; ■, Group 2, buprenorphine. * Indicates significant difference.

**Table 2.** Maximum change from baseline readings of blood pressure (systolic, mean, diastolic) heart rate and rate pressure product in the first 3 minutes after intubation. Values are expressed as mean (SEM).

| | Group 1 (saline) *n* = 20 | Group 2 (buprenorphine) *n* = 20 | p value |
|---|---|---|---|
| Systolic blood pressure | +40.2<br>(4.11) | +24.8<br>(3.54) | <0.01 |
| Mean blood pressure | +39.05<br>(4.26) | +24.68<br>(3.92) | <0.05 |
| Diastolic blood pressure | +37.5<br>(2.27) | +26.75<br>(2.25) | <0.01 |
| Heart rate | +22.95<br>(3.63) | +16.55<br>(3.03) | >0.05 |
| Rate pressure product | +7143<br>(896) | +4374<br>(574) | <0.05 |

2 hours after diazepam and Group 2 subjects were given buprenorphine 2.5 μg/kg intravenously in a blind fashion. Pre-oxygenation was started and continued for 3 minutes via a Magill system 5 minutes after the test medication. Anaesthesia was then induced in all patients with thiopentone 4 mg/kg, given over 15 seconds, followed by suxamethonium 1.5 mg/kg over 15 seconds to facilitate tracheal intubation, which was performed exactly 90 seconds after suxamethonium using a standard Macintosh blade. The patients' lungs were ventilated with 33% oxygen and 66% nitrous oxide to maintain normocapnia, during the period of apnoea. All intubations were done by the same anaesthetist and were accomplished within 15 seconds. Systolic, diastolic and mean arterial pressure, and heart rate were recorded after saline or buprenorphine bolus, following induction with thiopentone and suxamethonium, and at one-minute intervals after tracheal intubation, until spontaneous ventilation returned.

Student's *t*-test was applied for analysis of observations and a p value of less than 0.05 was considered significant.

## Results

*Demographic data.* There were no significant differences between the groups in respect of sex, mean age, weight, and baseline haemodynamic data (Table 1).

*Systolic arterial pressure.* The study medication did not cause a significant change in systolic arterial pressure. The systolic arterial pressure fell by an average of 6 mmHg following induction in the saline group and by 3 mmHg in those given buprenorphine compared to the baseline values, but the decrease was not significant.

A significant rise in systolic arterial pressure occurred immediately after intubation in patients who had received saline ($p < 0.001$). This persisted throughout the period of observation. A mean increase of 10 mmHg occurred immediately after intubation in the buprenorphine group, but this was not statistically significant from control. The rise of systolic arterial pressure became significant ($p < 0.01$) in this group during the second minute after intubation, but the readings at 3 minutes after intubation were again not significantly different from baseline values. The mean percentage changes compared to baseline values are shown in Figure 1.

The maximum increase from baseline values for heart rate, arterial pressure and rate pressure product are shown in Table 2. The maximum mean systolic arterial pressure following intubation was 177 mmHg, a rise of 29.4%, in those who received saline compared with 161.5 mmHg, a rise of 18.2%, in the buprenorphine group. This difference was significant ($p < 0.01$). Figure 2 shows the changes after intubation in both systolic and diastolic pressure.

*Diastolic arterial pressure (Fig. 2).* There was no significant change in diastolic arterial pressure after the study medication, but it increased after thiopentone in both groups and was statistically significant in the control group. After laryngoscopy and intubation, the diastolic arterial pressure increased maximally by 37.5 mmHg in the saline group (45%) and 26.75 mmHg (31.6%) in the buprenorphine group compared to baseline values. This difference between the two groups was significant (p value $< 0.01$).

*Heart rate.* The changes in heart rate are shown in Figure 3. Induction was accompanied by an increase in

P.24 526

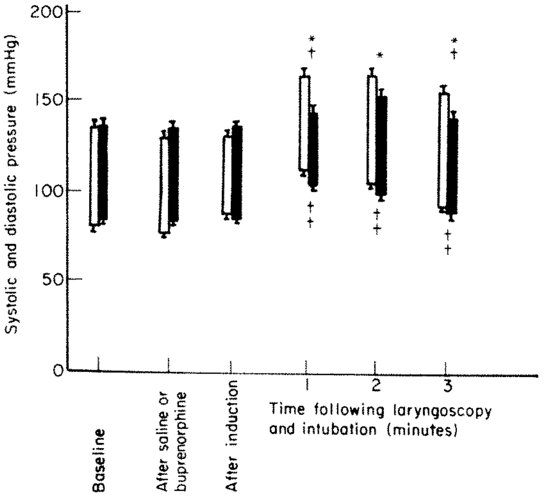


**Fig. 2.** Changes in the arterial pressure (mean, SEM) after tracheal intubation in patients who received intravenous saline (□) and buprenorphine (■) before induction. * Systolic blood pressure significantly different from baseline values; † systolic blood pressure significantly different from saline group; ‡ diastolic blood pressure significantly different from baseline values.

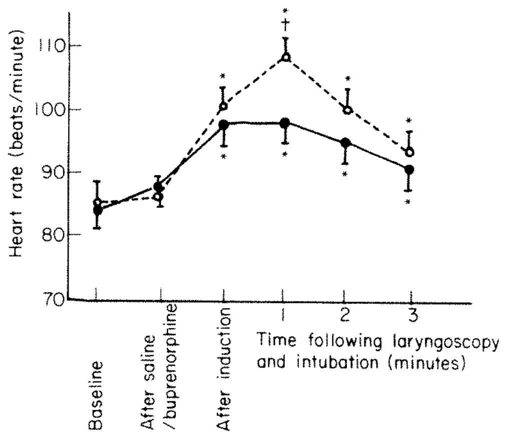


**Fig. 3.** Mean and SEM changes in the heart rate after tracheal intubation in patients who received intravenous saline (○) and buprenorphine (●) before induction of anaesthesia. * Significantly different from baseline values; † significantly different from saline group.

heart rate of 15 beats/minute in the control group ($p < 0.01$) compared to 12 beats/minute in the buprenorphine group ($p < 0.01$). There was no further change in heart rate after tracheal intubation in the buprenorphine group, but the heart rate increased further to 108 beats/minute in those given saline. Heart rate remained significantly elevated compared to control for a further 3 minutes after intubation in both groups.

*Rate pressure product.* Figure 4 shows the values for rate pressure product in the two groups. There was a significant rise in both groups at 1, 2 and 3 minutes after intubation. Maximum increase in the control group was 61.9% compared to the buprenorphine group, where the maximum rise was 37.2%. This difference was significant ($p < 0.05$).

*Maximum changes.* The maximum change from baseline readings of blood pressure, heart rate and rate pressure product in the first 3 minutes after intubation is shown in Table 2.

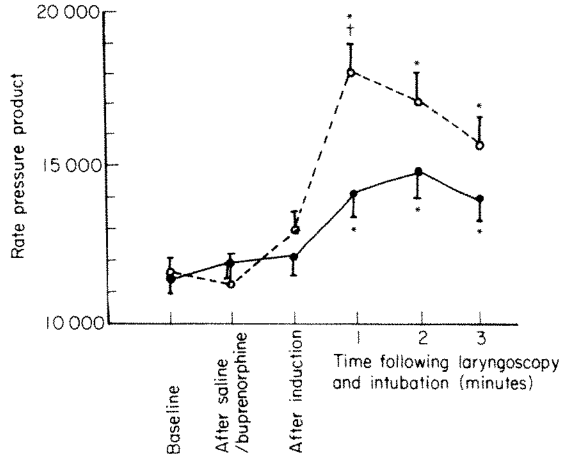


**Fig. 4.** Mean and SEM changes in the rate pressure product after tracheal intubation in patients who received intravenous saline (○) and buprenorphine (●) before induction of anaesthesia. * Significant difference from baseline values; † significant difference from saline group.

## Discussion

The hypertension and tachycardia associated with tracheal intubation following thiopentone and a depolarising relaxant is recognised as a potential cause of a number of complications. Intravenous narcotics have been used to attenuate these responses with variable degrees of success. Morphine, pethidine, nalbuphine, fentanyl, sufentanil and alfentanil have all been used.[18–21]

Fentanyl 5 μg/kg and alfentanil 40 μg/kg have both been successful in obtunding the reflex completely, but both have also been associated with profound hypotension and bradycardia, which were resistant to volume replacement and atropine, and an increased degree of respiratory depression.[18–20] Buprenorphine is a potent semisynthetic, centrally acting partial agonist opioid analgesic with a long duration of action.[25] Its intra-operative use for major surgery has been reported in a number of studies.[22,23,26,27] Its cardiovascular stability, longer duration of action and potential safety in overdosage outweighs its disadvantages, especially in major surgery after an intravenous dose of 0.3 mg. The onset of action is slow and its peak effect is between 2 and 10 minutes; the initial half life is 2 hours.[27–29] Different authors have recommended different dose regimens during anaesthesia.[22,23,26,27] We selected 2.5 μg/kg on the basis of a previous study done at our institution, which showed this dose to be adequate as a supplement in a balanced anaesthetic technique with minimal side effects in our patients. Some studies have reported on the slow pulse rate observed in some patients after buprenorphine.[27,30] This could be as a result of direct depression of conduction or a stimulant action on the vagal nucleus, similar to morphine. We chose to study the effects of buprenorphine on cardiovascular responses because of this property and its cardiostability.

Buprenorphine in the dose given attenuated the rise in systolic and diastolic arterial pressure associated with laryngoscopy and intubation. The heart rate showed significant increase compared to control values after thiopentone, which has been reported in other studies.[31,32] The heart rate in our patients did not decrease to the pre-induction levels before intubation, in contrast to the study by Harris *et al.*[31] There was a further increase in the pulse rate of 8% in the thiopentone group compared to 1% increase in the buprenorphine group on laryngoscopy and intubation.

The rate pressure product also showed an attenuated response after buprenorphine. The maximum mean rate pressure product after intubation in the buprenorphine group was 15 868. This compares favourably with a rate pressure product of 17 916 in response to intubation in patients given hydralazine before induction.[14]

In conclusion, therefore, in terms of the response to tracheal intubation, buprenorphine 2.5 μg/kg intravenously 8 minutes before induction provides relatively stable cardiovascular conditions compared to a standard induction technique where no narcotics are used.

## References

1. Tomori Z, Widdicombe JG. Muscular, bronchomotor and cardiovascular reflexes elicited by mechanical stimulation of the respiratory tract. *Journal of Physiology* 1969; **200:** 25–49.
2. Takeshima K, Noda K, Higaki M. Cardiovascular response to rapid anesthesia induction and endotracheal intubation. *Anesthesia and Analgesia* 1964; **43:** 201–4.
3. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: influence of duration of laryngoscopy with or without prior lidocaine. *Anesthesiology* 1977; **47:** 381–4.
4. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catacholamine responses to laryngoscopy with and without tracheal intubation. *British Journal of Anaesthesia* 1987; **59:** 295–9.
5. Low JM, Harvey JT, Prys-Roberts C, Dagnino J. Studies of anaesthesia in relation to hypertension. VII: Adrenergic response to laryngoscopy. *British Journal of Anaesthesia* 1986; **58:** 471–7.
6. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. *Anesthesiology* 1977; **47:** 524–5.
7. King BD, Harris LC, Greifenstein FE, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. *Anesthesiology* 1951; **12:** 556–66.
8. Miller AF, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. *British Journal of Anaesthesia* 1970; **42:** 618–24.
9. Fox E, Sklar GS, Hill C, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. *Anesthesiology* 1977; **47:** 524–5.
10. Burney RG, Winn R. Increased cerebrospinal fluid pressure during laryngoscopy and intubation for induction of anesthesia. *Anesthesia and Analgesia* 1975; **54:** 687–90.
11. Abou-Madi M, Keszler H, Yacoub O. A method for prevention of cardiovascular reaction to laryngoscopy and intubation, *Canadian Anaesthestists' Society Journal* 1975; **22:** 316–29.
12. Derbyshire DR, Smith G, Achola KJ. Effect of topical lignocaine on the sympathoadrenal response to tracheal intubation. *British Journal of Anaesthesia* 1987; **59:** 300–4.
13. Abou-Madi MN, Keszler H, Yacoub JM. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous doses of lidocaine. *Canadian Anaesthetists' Society Journal* 1977; **24:** 12–19.
14. Davis MJ, Cronin KD, Cowie RW. The prevention of hypertension at intubation. A controlled study of intravenous hydralazine on patients undergoing intracranial surgery. *Anaesthesia* 1981; **36:** 147–52.
15. Prys-Roberts C, Foex P, Biro GP, Roberts JG. Studies of anaesthesia in relation to hypertension. V: Adrenergic beta-receptor blockade. *British Journal of Anaesthesia* 1973: **45:** 671–80.
16. Kamra S, Wig J, Sapru RP. Topical nitroglycerin. A safeguard against pressor responses to tracheal intubation. *Anaesthesia* 1986; **41:** 1087–91.
17. Curren J, Crowley M, O'Sullivan G. Droperidol and endotracheal intubation. Attenuation of pressor response to laryngoscopy and intubation. *Anaesthesia* 1980; **35:** 290–4.
18. Kay B, Healy TEJ, Bolder PM. Blocking the circulatory responses to tracheal intubation. A comparison of fentanyl and nalbuphine. *Anaesthesia* 1985; **40:** 960–3.
19. Kay B, Nolan D, Mayall R, Healy TEJ. The effect of sufentanil on the cardiovascular responses to tracheal intubation. *Anaesthesia* 1987; **42:** 382–6.
20. Crawford DC, Fell D, Achola KJ, Smith G. Effects of alfentail on the pressor and catecholamine responses to tracheal intubation. *British Journal of Anaesthesia* 1987; **59:** 707–12.
21. Flacke JW, Bloor BC, Kripke BJ, Flacke WE, Warneck CM, Van Etten AP, Wong DH, Katz RL. Comparison of morphine, meperidine, fentanyl and sufentanil in balanced anaesthesia: a double-blind study. *Anesthesia and Analgesia* 1985; **64:** 897–910.
22. Green DW, Sinclair JR, Mikhael MS. Buprenorphine versus morphine. A comparison of intra-operative and postoperative analgesia. *Anaesthesia* 1985; **40:** 371–5.
23. Abrahamson J, Niemand D, Olsson AK, Tornebandt K. Buprenorphine (Temgesic) as a peroperative analgesic. A multicenter study. *Anaesthesist* 1983; **32:** 75–9.
24. Foëx P, Prys-Roberts C. Anaesthesia and the hypertensive patient. *British Journal of Anaesthesia* 1974; **46:** 575–88.
25. Heel RC, Brogden RN, Speight TM, Avery GS. Buprenorphine: a review of its pharmacological properties and therapeutic efficacy. *Drugs* 1979; **17:** 81–110.
26. Bevan PLT, Macnee CM, Orwin JM. An open multicentre study of buprenorphine used as the sole analgesic in the pre, per and post operative periods. In: Paul L, Bevan T, Firsh M, eds. *Buprenorphine and anaesthesiology.* Royal Society of Medicine International Congress and Symposium Series No. 65, Royal Society of Medicine, 1984; 89–94.
27. Kay B. A double-blind comparison between fentanyl and buprenorphine in analgesic-supplemented anaesthesia. *British Journal of Anaesthesia* 1980; **52:** 453–6.
28. Bullingham RES, McQuay HJ, Moore A, Bennett MRD. Buprenorphine kinetics. *Clinical Pharmacology and Therapeutics* 1980; **28:** 667–72.
29. Cowan A, Lewis JW, Macfarlane IR. Agonist and antagonist properties of buprenorphine, in new antinociceptive agents. *British Journal of Pharmacology* 1977; **60:** 537–41.
30. Downing JW, Leary WP, White ES. Buprenorphine: A new potent long-acting synthetic analgesic. Comparison with morphine. *British Journal of Anaesthesia* 1977; **49:** 251–5.
31. Harris CE, Murray AM, Anderson JM, Grounds RM, Morgan M. Effects of thiopentone, etomidate and propofol on the haemodynamic response to tracheal intubation. *Anaesthesia* 1988; **43:** (Suppl.) 32–6.
32. Boralessa H, Senior DF, Whitwam JG. Cardiovascular response to intubation. A comparative study of thiopentone and midazolam. *Anaesthesia* 1983; **38:** 623–7.

*Anaesthesia*, 1989, Volume 44, pages 398–399

# Stellate ganglion block with bupivacaine

## Minimum effective concentration of bupivacaine and the effect of added potassium

P. A. J. HARDY

### Summary

*Sympathetic blockade after stellate ganglion block with bupivacaine was assessed by liquid crystal thermography. The minimum concentration of bupivacaine required for successful block was between 325 and 406 μmol/litre. Further study of bupivacaine in a solution that contained potassium 5 mmol/litre showed that this reduced the minimum concentration of bupivacaine required for successful block to between 81 and 162 μmol/litre. We conclude that potassium has a major effect on the minimum concentration of bupivacaine required for sympathetic blockade.*

**Key words**

*Anaesthetic techniques*; regional, stellate ganglion.
*Anaesthetics, local*; bupivacaine.

Several factors may influence local anaesthetic drug action. One which has received repeated attention is the addition of potassium to the injectate. Potassium alone may inhibit action potentials.[1] Various effects have been noted when potassium is added to local anaesthetic solutions.[2] The speed of onset of prilocaine but not bupivacaine may be enhanced[3] and the duration of blockade may be prolonged by the addition of potassium.[4,5]

The cervical sympathetic chain contains a mixture of pre- and postganglionic fibres that lie freely over the precervical fascia in the neck. Previous study has shown that a volume of 20 ml of bupivacaine was required to block all sympathetic fibres to the hand[6] when assessed by liquid crystal thermography. A study was performed using this 'model' to assess the minimum concentration of bupivacaine required to produce sympathetic blockade, and the effect of added potassium (5 mmol/litre).

### Method

Stellate ganglion block was performed on 20 patients as part of the treatment of chronic pain conditions that affected the head, neck and arm. The patients were informed of the nature of the studies, that sympathetic blockade might not occur and that a repeat block would be offered in the event of failure to produce a block or poor analgesia.

A standard anterior approach to the sympathetic chain over the precervical fascia at $C_6$ was used with the patient supine and with the neck extended. The patients were encouraged to sit up after injection to encourage spread of injectate. A volume of 20 ml was used in each patient. The first 10 patients received a solution that contained bupivacaine in sodium chloride. The first patient received bupivacaine 0.5% (16 200 μmol/litre), the second patient 0.1% and subsequent patients received progressively lower concentrations until no sympathetic block occurred; four further patients then received concentrations above or below this threshold value. The next 10 patients received bupivacaine with added potassium in a concentration of 5 mmol/litre. The first two patients received bupivacaine in a concentration equal to that just above the threshold value in the first series; two patients each received progressively lower concentrations until sympathetic block failed to occur.

A Novatherm (Novamedix) contact thermography system was used to assess skin temperature. This system employs latex detectors with the internal face coated with a layer of micro-encapsulated cholesterol stearate liquid crystals. The crystals reflect incident light, and thermal rotation of the crystal 'stacks' refracts the light wave to produce a colour which is determined by the temperature applied to the detector. There is a series of detectors, each with a range of 4°C and with 50% overlap between adjacent detectors; thus the system is applicable to a temperature range of 20 to 38°C. The sensitivity of the system is 0.8°C.

Thermal images of the hands were taken before and 30

---

P.A.J. Hardy, BSc, MB, ChB, FFARCS, Clinical Research Fellow, Pain Relief Foundation, Rice Lane, Liverpool L9 1AE.

Accepted 22 November 1988.

0003–2409/89/050398 + 02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

minutes after the injection. This interval had been shown previously to be that at which maximum sympathetic blockade is present after injection of bupivacaine.[7] The patients remained clothed in a draught-free room with an environmental temperature of 20 to 22°C during the study period. A positive sympathetic block was determined by an increase in ipsilateral hand temperature of at least 1.6°C; the block was confirmed by proximal application of ice.[8]

## Results

A serial decrease in concentration of bupivacaine down to 406 µmol/litre produced positive sympathetic blockade (Table 1). This was confirmed on three occasions. Blockade did not occur in any of the three patients who received a concentration of 325 µmol/litre.

**Table 1.** Concentration of bupivacaine and sympathetic blockade.

| Bupivacaine concentration | | Sympathetic block | |
|---|---|---|---|
| % | µmol/litre | plain | + KCl 5 mmol/litre |
| 0.5 | 16200 | + | |
| 0.1 | 3250 | + | |
| 0.05 | 1625 | + | |
| 0.025 | 812 | + | |
| 0.0125 | 406 | + + + | + + |
| 0.01 | 325 | − − − | + + |
| 0.0075 | 244 | | + + |
| 0.005 | 162 | | + + |
| 0.0025 | 81 | | − − |

+, successful sympathetic block. −, unsuccessful sympathetic block. Each symbol represents one patient.

Addition of potassium chloride to the previous minimum concentration again resulted in sympathetic blockade. Further serial dilutions of bupivacaine down to 162 µmol/litre bupivacaine with potassium 5 mmol/litre also produced sympathetic blockade (Table 1). There was no sympathetic block at a concentration of 81 µmol/litre.

All patients reported analgesia after the block had been performed.

## Discussion

The presence of Horner's complex (ptosis, miosis and enophthalmos) is often used as an indication of sympathetic blockade after stellate ganglion block; however, this may occur after a 'placebo' injection of sodium chloride solution.[9] This effect may be due to the presence of preservatives in the solution (e.g. benzyl alcohol, which does possess local anaesthetic activity);[10] however, sodium chloride may produce segmental hypo-aesthesia after intrathecal injection.[11] Pressure effects from the injectate may result in neural dysfunction and may produce 'sympathetic block'. Preservative-free solutions were used in this study, but ionic or pressure effects may have played a role in the results observed.

Previous *in vitro* studies using desheathed nerve preparations have defined minimum blocking concentration of amide[12] and ester[13] local anaesthetics. A minimum concentration of bupivacaine of 110 µmol/litre was found to block $A\delta$ and B fibres while a concentration of 210 µmol/litre was required to block C fibres.[14] A bathing solution that contained potassium was used in these studies. The minimum effective concentration of plain bupivacaine was between 325 and 406 µmol/litre in the present study, whereas in the presence of potassium 5 mmol/litre the minimum concentration was between 81 and 162 µmol/litre. The latter range is similar to the concentration required to block $A\delta$ and B fibres *in vitro*[14] and is well below that required to block C fibres. Preganglionic autonomic fibres are in the B fibre group while postganglionic (unmyelinated) fibres are in the C fibre group. It is possible, if similar blocking concentrations exist in man as in the desheathed rabbit vagus nerve, that the sympathetic nerve blockade produced in the hand after stellate ganglion block is preganglionic in origin.

## Acknowledgments

I thank Imperial Chemical Industries plc for financial support.

## References

1. Huxley AF, Stämpfli R. Effect of potassium and sodium on resting and action potentials of single myelinated nerve fibres. *Journal of Physiology* 1951; **112:** 496–508.
2. Bromage PR, Burfoot MF. Quality of epidural blockade. II: Influence of physico-chemical factors; hyaluronidase and potassium. *British Journal of Anaesthesia* 1966; **38:** 857–65.
3. Parris MR, Chambers WA. Effects of the addition of potassium to prilocaine or bupivacaine. Studies on trachial plexus blockade. *British Journal of Anaesthesia* 1986; **58:** 297–300.
4. Aldrete JA, Barnes DR, Sidon MA, Mcmullen RB. Studies on effects of addition of potassium chloride to lidocaine. *Anesthesia and Analgesia* 1969; **48:** 269–76.
5. Kircha S, Barsa J, Fink BR. Potentiation of nerve block in vivo by physiological adjuvants in the solution. *British Journal of Anaesthesia* 1983; **55:** 549–53.
6. Hardy PAJ, Wells JCD. Extent of sympathetic blockade after stellate ganglion block with bupivacaine. *Pain* 1989; (in press).
7. Eriksen S. Duration of sympathetic blockade. Stellate ganglion versus intravenous regional guanethidine block. *Anaesthesia* 1981; **36:** 768–71.
8. Hardy PAJ. Quantification of sympathetic blockade by thermography. *British Journal of Anaesthesia* 1987; **59:** 664–5.
9. Rattenborg CC, Lichtor JL, Lorincz AL. Stellate ganglion blockade after 'placebo' injection. *New England Journal of Medicine* 1983; **309:** 433.
10. Wightman MA, Vaughan RW. Comparison of compounds used for intradermal anesthesia. *Anesthesiology* 1976; **45:** 687–9.
11. Urban BJ, McKain CW. Local anesthetic effect of intrathecal normal saline. *Pain* 1979; **5:** 43–52.
12. Gissen AJ, Covino BG, Gregus, J. Differential sensitivities of mammalian nerve fiber to local anesthetic agents. *Anesthesiology* 1980; **53:** 467–74.
13. Wildsmith JAW, Gissen AJ, Gregus J, Covino BG. Differential nerve blocking activity of amino-ester local anaesthetics. *British Journal of Anaesthesia* 1985; **57:** 612–20.
14. Covino BG. The mechanism of local anaesthesia. In: Norman J, Whitwam J, eds. *Topical reviews in anaesthesia, Vol. 1.* Bristol: Wright, 1980: 85–134.

*Anaesthesia*, 1989, Volume 44, pages 400–403

# Epidural diamorphine and bupivacaine in labour

E. M. McGRADY, D. K. BROWNHILL AND A. G. DAVIS

## Summary

*A double-blind randomised study was performed to assess the analgesic effect of epidural diamorphine, administered with bupivacaine, on primigravid women in labour. Fifty patients received 0.25% bupivacaine 10 ml via the epidural catheter as their initial dose; patients in Group 1 received diamorphine 5 mg with the bupivacaine. A 0.1% bupivacaine infusion was started at 10 minutes and bolus doses of bupivacaine were given if required. There was a significant reduction in rate of bupivacaine administration, pain scores at 20 and 30 minutes, number of supplements required, and degree of motor blockade in the diamorphine group.*

## Key words

*Anaesthetic techniques, regional*; epidural.
*Analgesia*; obstetric.

Local anaesthetic agents administered through the epidural route are known to provide excellent analgesia in labour. However, associated side effects may prove troublesome, notably lower limb weakness and hypotension, due to concomitant motor and sympathetic blockade. Excessive dosage may lead to systemic toxicity.

Epidural opioids can provide prolonged 'selective' analgesia and avoid the side effects of local anaesthetic agents. Epidural morphine, however, when used as the sole analgesic agent in this way in labour, showed disappointing results, particularly in relieving the pain of the second stage.[1–4] Techniques that use a mixture of bupivacaine and fentanyl have proved more encouraging; for example fentanyl administered with a test dose of bupivacaine improved the quality of analgesia and reduced bupivacaine requirements throughout labour, although the incidence of bupivacaine-related side effects remained unchanged.[5–7] A single dose of epidural fentanyl provided analgesia for a mean of 3.83–5.7 hours in postoperative patients[8,9], a duration of action which may be inadequate in labour. Diamorphine acts for longer, with mean durations of 6–12 hours,[8,9] and shares the lipophilicity of fentanyl, which is desirable for epidural use.

We postulated that the administration of diamorphine with bupivacaine to women in labour might improve the quality of analgesia and reduce bupivacaine dosage and associated side effects. The aim of this study was to assess the analgesic effect of a single dose of epidural diamorphine, administered with bupivacaine, on primigravid women in the first stage of labour.

## Methods

Fifty primigravid women who requested epidural analgesia in the first stage of labour were investigated. The hospital ethics committee had approved the study and written consent was obtained. Mothers who had already received opioid analgesia in labour or those with cervical dilatation of more than 4 cm at the last examination were not studied. Two operators were required for the study; one prepared the solution to be administered epidurally while the other sited the epidural, administered the prepared solution, and completed the data sheet for that patient.

Mothers received a litre of compound sodium lactate solution intravenously during the insertion of an epidural catheter at the $L_{2/3}$ interspace; 3–4 cm was left in the space. They were randomly allocated into one of two groups for the double-blind administration of either diamorphine 5 mg dissolved in 10 ml 0.25% plain bupivacaine (Group 1), or 10 ml 0.25% plain bupivacaine alone (Group 2). The injection was made over 5 minutes; 5 ml administered in the left lateral position and the patient turned at 5 minutes to receive 5 ml on the right side. Ten minutes after the initial dose, a continuous infusion of 0.1% plain bupivacaine was started at the rate of 10 ml per hour. Supplementary doses of 0.25% bupivacaine 10 ml were

---

E.M. McGrady,* FFARCS, Senior Registrar, D.K. Brownhill, FFARCS, Registrar, A.G. Davis, FFARCS, Consultant, Department of Anaesthetics, Southern General Hospital, Glasgow.
* Present appointment: Senior Registrar, Western Infirmary, Glasgow.
Accepted 12 October 1988.

0003–2409/89/050400 + 04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Patient data. Values expressed as mean (SD) or (range).

| | Group 1 | Group 2 |
|---|---|---|
| Height, m | 1.6 (5.9) | 1.6 (5.6) |
| Weight, kg | 71.5 (11.5) | 73.5 (11.6) |
| Duration of labour after epidural sited, hours | 6.6 (2.3–11.7) | 6.1 (1.5–12.2) |

**Table 2.** Rate of bupivacaine administration throughout labour, and number of bupivacaine supplements required.

| | Group 1 | Group 2 | |
|---|---|---|---|
| Rate of bupivacaine administration, mean, range) | | | |
| mg/hour | 16.7<br>(12.6–33.0) | 21.8<br>(12.7–40.2) | $p < 0.01$ |
| mg/kg/hour | 0.23<br>(0.15–0.35) | 0.3<br>(0.16–0.51) | $p < 0.01$ |
| Number of supplements | | | |
| 0 | 15 | 4 | |
| 1 | 3 | 6 | |
| 2 | 2 | 7 | |
| 3 | 2 | 4 | |
| 4 | 1 | 1 | |
| | $p < 0.01$ | | |

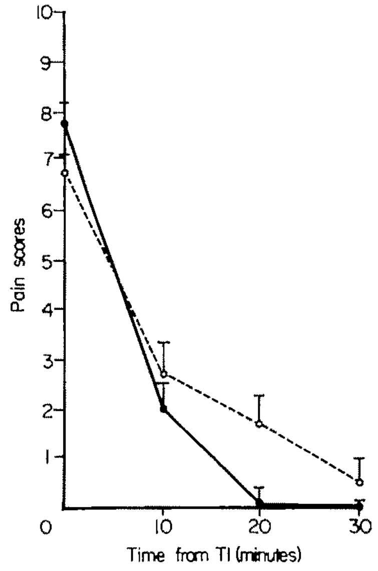


**Fig. 1.** Reduction in pain score after first epidural injection ($T_1$). Mean plus SEM (vertical bar). ---○---, control group; ——●——, diamorphine group.

**Table 3.** Incidence of side effects.

| | Group 1 | Group 2 | |
|---|---|---|---|
| Hypotension (systolic < 100 mmHg) | 6 | 5 | |
| Itching | 18 | 0 | $p < 0.01$ |
| Urinary retention | 7 | 7 | |
| Nausea/vomiting | 15 | 8 | |
| Respiratory depression | 0 | 0 | |

given if required throughout labour; if this proved inadequate, 0.5% bupivacaine 10 ml was administered.

Pain scores were assessed using a 10-cm visual analogue scale as recommended by Scott and Huskisson;[10] measurement was taken before insertion of the epidural, and at 10, 20, and 30 minutes after the initial dose. Time till the first painless contraction was noted. The total dose of bupivacaine administered throughout labour was recorded and its rate of administration calculated. Any associated side effect of either diamorphine or bupivacaine was recorded, e.g. hypotension (defined as systolic blood pressure < 100 mmHg), itch, nausea or vomiting. The severity of motor blockade was assessed every 2 hours using the following criteria: 0, no weakness; 1, able to raise straight leg; 2, able to slide leg up bed by bending knee; 3, unable to flex knee. The height of the sensory block, using loss of cold sensation, was measured 2 hourly. The Apgar score of the infant and the mode of delivery were both noted.

Statistical analysis was performed using the Mann–Whitney *U* and Fischer exact probability tests as appropriate. A p value less than 0.05 was taken to be significant.

## Results

The groups were comparable for height, weight and duration of labour after the epidural was sited (Table 1). Fifty patients participated in the study although five were subsequently withdrawn and will be discussed later.

### *Bupivacaine dosage*

The rate of bupivacaine administration was found to be significantly lower in the diamorphine group (Table 2). Fifteen mothers in Group 1 required no further supplements compared with four in Group 2, and overall significantly fewer top-ups were required in the diamorphine group (Table 2). One patient in Group 1 required four supplements; she was found to have an unblocked segment which was partially relieved when the epidural was resited.

### *Onset of analgesia*

The mean time till first painless contraction was longer in the control group, 22.5 minutes (range 6–60), than in Group 1, 11.9 minutes (range 5–35), but the difference did not reach statistical significance. However pain scores were lower in the diamorphine group and this reached significant levels 20 and 30 minutes after the initial dose (Fig. 1).

### *Side effects*

The incidence of side effects is presented in Table 3 and shows similar figures for hypotension, urinary retention, nausea and vomiting. There were no cases of either early or late respiratory depression. Eighteen women in the diamorphine group experienced itching, and of these in 14 it was elicited only by direct questioning; only two patients found it troublesome.

### *Motor blockade*

The most profound degree of block throughout labour was recorded for each patient. Seventeen patients in the diamorphine group experienced only minimal weakness i.e. grade 1 or 0, compared with six in the control group, and this difference is significant ($p < 0.01$).

*Perineal/sacral pain*

Seven patients in the control group complained of distressing low back or perineal discomfort only partially relieved by bupivacaine supplements. A further three patients in the control group were withdrawn from the study and are not included in the statistical analysis; all three experienced severe perineal/sacral pain unrelieved by supplementary doses of bupivacaine. Epidural opioids are particularly effective in relieving this type of pain. The code was broken as it seemed likely that these patients were in the control group, and they subsequently received epidural opioids with satisfactory result. The increased incidence of perineal pain is significant at the 5% level. This was an incidental finding in the study, since patients were not specifically asked about this type of pain; if they complained of persistent discomfort this was noted.

There was no difference between the groups for mode of delivery. Apgar scores were similar at 1 and 3 minutes; 16 in Group 1 and 15 in Group 2 were greater than or equal to nine at one minute, with 23 and 20 respectively at 3 minutes. All mothers were reviewed on the first postnatal day to assess maternal satisfaction with the technique; the majority had found the epidural to be entirely satisfactory. The maximum height of sensory loss to cold sensation was $T_6$ in Group 1 (range $T_{10}$–$T_6$), and $T_4$ in group 2 (range $T_{10}$–$T_4$).

## Discussion

The study has demonstrated that diamorphine is a useful adjunct to epidural bupivacaine in labour, and results in reductions in the rate of bupivacaine administration, degree of motor blockade, number of supplements required, and a faster reduction in pain scores. The incidence of perineal/sacral pain appeared to be diminished.

Diamorphine, in common with fentanyl, is a lipophilic opioid with a faster onset time than morphine. Once absorbed into the cerebrospinal fluid, lipophilic opioids rapidly enter the spinal cord; there will be only a low concentration of diamorphine in the CSF, reducing the potential for delayed respiratory depression.[9] *In vitro* work suggests molecular weight, rather than lipophilicity, is the major factor to influence rate of dural penetration,[11] but *in vivo* work suggests opioids gain access to the subarachnoid space via arachnoid granulations in the dural cuff region and penetrating radicular arteries, in addition to penetration of the dura.[9] Therefore lipophilic opioids have a more rapid onset of action regardless of molecular weight, although fentanyl is most rapid because of its molecular shape.[9]

An unknown proportion of epidural opioid is absorbed into epidural veins, and this limits the amount available for a spinal action and probably contributes to the early stage of analgesia. The proportion entering the systemic circulation will increase with lipophilicity and is likely to be higher in the pregnant patient with her increased epidural blood flow. It has been suggested that epidural diamorphine is merely an exotic way of administering a systemic opioid.[12] Vella and co-workers[13] administered epidural fentanyl with bupivacaine to women in labour and compared the technique with controls who received an intravenous infusion designed to produce comparable plasma fentanyl concentrations. Analgesia was more complete, rapid and of longer duration in the epidural fentanyl group, despite higher fentanyl levels in the control group. They concluded that systemic absorption of fentanyl had contributed little to the analgesia. Diamorphine has not been investigated in this way, but it does have a longer duration of action when given epidurally rather than systemically in the nonpregnant patient.[12,14] It seems likely that a significant degree of analgesia is the result of a selective spinal effect.

Justins and co-workers[6] report fentanyl and bupivacaine mixtures to be particularly effective in the relief of persistent perineal pain, and diamorphine appears to share this property. Only one patient in the diamorphine group complained of this. How epidural opioids relieve this type of pain is unclear; presumably it is due to the additive effect observed in local anaesthetic/opioid mixtures of afferent neural blockade, selective spinal analgesia and a central spinal effect.[15]

One of the initial aims of this study was to reduce the incidence of local anaesthetic-related side effects, and indeed the severity of motor blockade was diminished in the diamorphine group, which must improve patient mobility and comfort. There was no reduction in the incidence of instrumental delivery associated with this, but the question of whether epidural analgesia increases forceps rate is a controversial one. Comparable numbers of patients experienced hypotension in the two groups; similar work with fentanyl demonstrated variable effects on the incidence of hypotension.[6,16]

Side effects attributable to epidural opioid administration were also noted. More patients in Group 1 experienced nausea and vomiting though this was not statistically significant; three patients in Group 1 and one in Group 2 required prochlorperazine administration. Itching occurred in 18 Group 1 mothers, but most did not find it troublesome. One woman found it severe and this was relieved by intravenous naloxone 0.4 mg with no diminution in degree of analgesia.

A major anxiety when epidural opioids are administered is their potential to cause early or late respiratory depression. Recognised risk factors are old age, poor general health, use of hydrophilic opioids, concomitant administration of systemic opioids, and marked changes in thoraco-abdominal pressure, including artificial ventilation.[9,17] The incidence of this complication is unclear; one survey reported a delayed respiratory depression rate of 1 in 1 100 (0.09%), after epidural morphine administration; risk factors were present in all the patients.[17]

Evidence suggests that the ventilatory depressant effect of diamorphine may be maximal early rather than late, and occur in patients with the risk factors mentioned above.[14,18–20] All the patients in our study were monitored closely during labour and for some hours postnatally; no risk factors were present, and any woman who had already received systemic opioid was excluded. Respiratory rate was not measured; all the patients were awake and respiratory rate may not be a good indicator for respiratory depression.[20] Caution should be exercised until more information is available on the use of epidural diamorphine and its effect on ventilation 6–12 hours after its administration. Nine patients in the diamorphine group experienced drowsiness; most found it pleasant, though in one mother it lasted for 12 hours and she felt it had interfered with feeding the baby. Perhaps a smaller dose, e.g. diamorphine 3 mg might limit some of the side effects.

Three patients in the diamorphine group, who required two or more supplements, had labours that lasted longer than 8 hours, and possibly the diamorphine effect had worn off. Women with shorter labours found analgesia to be satisfactory throughout the second stage. Administration of opioid and local anaesthetic mixtures via epidural infusion may avoid this problem; fentanyl and bupivacaine provided excellent analgesia in the first and second stage when given by this method.[21] Epidural infusion of diamorphine and bupivacaine mixtures are reported to provide good postoperative analgesia; and are significantly superior to either agent used alone.[15,22] Avoiding the use of a bolus of opioid may diminish the risk of early respiratory depression.

In conclusion, the addition of diamorphine to the initial dose of bupivacaine reduced the rate of bupivacaine administration and the number of supplements required throughout labour; the degree of motor blockade was lessened and there were fewer complaints of perineal/sacral pain. The incidence of itching was high but almost always mild. Some mothers felt drowsy, but there were no cases of early or late ventilatory depression.

## References

1. Hughes SC, Rosen MA, Shnider SM, Abboud TK, Stefani SJ, Norton M. Maternal and neonatal effects of epidural morphine for labor and delivery. *Anesthesia and Analgesia* 1984; **63:** 319–24.
2. Crawford JS. Experiences with epidural morphine in obstetrics. *Anaesthesia* 1981; **36:** 207–9.
3. Booker PD, Wilkes RD, Bryson THL, Beddard J. Obstetric pain relief using epidural morphine. *Anaesthesia* 1980; **35:** 377–9.
4. Husemeyer RP, O'Connor MC, Davenport HT. Failure of epidural morphine to relieve pain in labour. *Anaesthesia* 1980; **35:** 161–3.
5. Francis DM, Justins D, Reynolds FJM. Obstetric pain relief using epidural narcotic agents. *Anaesthesia* 1981; **36:** 69.
6. Justins DM, Francis D, Houlton PG, Reynolds F. A controlled trial of extradural fentanyl in labour. *British Journal of Anaesthesia* 1982; **54:** 409–14.
7. Justins DM, Knott C, Luthman JH, Reynolds F. Epidural versus intramuscular fentanyl. Analgesia and pharmacokinetics in labour. *Anaesthesia* 1983; **38:** 937–42.
8. Houlton PG, Reynolds F. Epidural diamorphine and fentanyl for postoperative pain. *Anaesthesia* 1981; **36:** 1144–5.
9. Cousins MJ, Mather LE. Intrathecal and epidural administration of opioids. *Anesthesiology* 1984; **61:** 276–310.
10. Scott J, Huskisson EC. Graphic representation of pain. *Pain* 1976; **2:** 175–84.
11. Moore RA, Bullingham ES, McQuay HJ, Hand CW, Aspel JB, Allen MC, Thomas D. Dural permeability to narcotics: *in vitro* determination and application to extradural administration. *British Journal of Anaesthesia* 1982; **54:** 1117–28.
12. Jacobson L, Phillips PD, Hull CJ, Conacher ID. Extradural versus intramuscular diamorphine. A controlled study of analgesic and adverse effects in the postoperative period. *Anaesthesia* 1983; **38:** 10–18.
13. Vella LM, Willatts DG, Knott C, Lintin DJ, Justins DM, Reynolds F. Epidural fentanyl in labour. An evaluation of the systemic contribution to analgesia. *Anaesthesia* 1985; **40:** 741–7.
14. Malins AF, Goodman NW, Cooper GM, Prys-Roberts C, Baird RN. Ventilatory effects of pre- and postoperative diamorphine. A comparison of extradural and intramuscular administration. *Anaesthesia* 1984; **39:** 118–25.
15. Lee A, Simpson D, Whitfield A, Scott DB. Postoperative analgesia by continuous extradural infusion of bupivacaine and diamorphine. *British Journal of Anaesthesia* 1988; **60:** 845–50.
16. Youngstrom P, Eastwood D, Patel H, Bhatia R, Cowan R, Sutheimer C. Epidural fentanyl and bupivacaine in labor: double blind study. *Anesthesiology* 1984; **61:** A414.
17. Rawal N, Arner S, Gustafsson LL, Allvin R. Present state of extradural and intrathecal opioid analgesia in Sweden. A nationwide follow-up survey. *British Journal of Anaesthesia* 1987; **59:** 791–9.
18. Cooper GM, Goodman NW, Prys-Roberts C, Jacobson L, Douglas G. Ventilatory effects of extradural diamorphine. *British Journal of Anaesthesia* 1982; **54:** 239P.
19. Watson J, Moore A, McQuay A, Teddy P, Baldwin D, Allen M, Bullingham R. Plasma morphine concentrations and analgesic effects of lumbar extradural morphine and heroin. *Anesthesia and Analgesia* 1984; **63:** 629–34.
20. Grant IS. Drowsiness after epidural opioids. *Anaesthesia* 1986; **41:** 431–2.
21. Skerman JH, Thompson BA, Goldstein MT, Jacobs MA, Gupta A, Blass NH. Combined continuous epidural fentanyl and bupivacaine in labor: a randomised study. *Anesthesiology* 1985; **63:** A450.
22. Prys-Roberts C. Anaesthesia and severe pulmonary disease. *British Journal of Hospital Medicine* 1986; **35:** 43–5.

*Anaesthesia*, 1989, Volume 44, pages 404–405

CASE REPORT

# Cardiovascular instability following bolus dose of etomidate

E. M. McGRADY AND I. H. WRIGHT

## Summary

*A patient with alveolar proteinosis developed unexpected cardiovascular instability after broncho-alveolar lavage. He had received two bolus doses of etomidate within an 18-hour period. Serum cortisol concentrations were low and hydrocortisone replacement therapy was necessary to restore arterial pressure. Implications for management of critically ill patients who receive bolus doses of etomidate are discussed.*

## Key words

*Anaesthetics, intravenous*; etomidate.
*Complications*; hypotension.

Ledingham and Watt noticed an increased mortality in Intensive Therapy Unit (ITU) patients who received an infusion of etomidate, and suggested suppression of adrenocortical function as a possible mechanism to explain this effect.[1,2] Subsequently, various groups identified intramitochondrial enzyme inhibition as the cause of decreased cortisol concentrations.[3–6] The mechanism of the increased mortality is unclear but in addition to the well known electrolyte changes associated with low cortisol concentrations, Barton and Little identified an inability to compensate for fluid loss in rats treated with an inhibitor of adrenal steroidogenesis, and discussed the role of glucocorticoids in potentiation of the vasoconstrictor effects of catecholamines.[7]

Owen and Spence reviewed the evidence for adrenal suppression after a bolus dose of etomidate.[8] They concluded that a bolus dose of etomidate did cause temporary adrenocortical suppression, but no harmful effect had been demonstrated, and the advantages of etomidate outweighed this theoretical risk.

We describe a patient who received two doses of etomidate as an anaesthetic induction agent within an 18-hour period. His postoperative recovery was complicated unexpectedly by a period of cardiovascular instability.

## Case history

A 45-year-old man who weighed 80 kg was admitted for elective bronchial lavage under general anaesthesia; the diagnosis of alveolar proteinosis was made some months earlier. The patient was well, except for steadily increasing dyspnoea and chronic hypoxaemia ($P\text{a}O_2$ 8.7 kPa while breathing air).

Anaesthesia was induced with etomidate; 20 mg was inadequate and a further dose of 20 mg was administered. Suxamethonium provided muscle relaxation and a left-sided double-lumen bronchial tube was inserted. Subsequently he received alcuronium 30 mg and midazolam 10 mg during a 90-minute procedure in which the right lung was lavaged with 10 litres of isotonic saline. Transient arterial desaturation occurred when the lung was lavaged, but his cardiovascular system remained stable. He was transferred to the ITU for postoperative pulmonary ventilation.

Gas exchange was poor initially ($P\text{a}O_2$ 6.1 kPa, $F\text{I}O_2$ 0.5), and ventilation was continued overnight; sedation was provided with morphine and midazolam. The following morning, arterial blood gases remained unsatisfactory and the double-lumen tube was exchanged for a single-lumen tracheal tube; etomidate 30 mg was administered for this procedure. Cardiovascular variables were stable before this, but systolic arterial pressure decreased to 60 mmHg over the next hour. Colloid infusion restored the pressure initially, but it remained unstable throughout the day, despite an adequate central venous pressure and improved oxygenation ($P\text{a}O_2$ 22.7 kPa, $F\text{I}O_2$ 0.5). A dobutamine infusion was started 14 hours after the second dose of etomidate because of continued hypotension; arterial pressure was restored to a reasonable level.

The patient's electrocardiogram was unchanged throughout his admission, and there was no evidence of sepsis. The serum cortisol concentration measured in a blood sample

---

E.M. McGrady, FFARCS, Senior Registrar, I.H. Wright,* MRCP, FFARCS, Registrar, Department of Anaesthetics, Western Infirmary, Dumbarton Road, Glasgow G11 6NT.
*Present appointment: Senior Registrar, Department of Anaesthetics, Bristol Royal Infirmary.

Accepted 31 October 1988.

0003–2409/89/050404 + 02 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

taken 16.5 hours after the initial dose of etomidate and before the second, was low (82 nmol/litre; normal range 350–700 nmol/litre). Hydrocortisone 100 mg was administered and colloid was transfused; this resulted in transient improvement in arterial pressure. The serum cortisol concentration remained very low on the second postoperative day (62 nmol/litre 21 hours after the second dose of etomidate); a further dose of hydrocortisone 100 mg was given. Cardiovascular variables stabilised during the day and inotropic support was discontinued. The serum cortisol concentration increased to 178 nmol/litre on the third day and no further steroid was administered. Subsequent recovery was rapid, and the patient returned to the ward.

A short Synacthen test performed on the first postoperative day was unfortunately inconclusive, because hydrocortisone was administered beforehand. The test was repeated 4 days later in the ward and was normal. Serum electrolyte concentrations were unremarkable during admission except for the presence of a potassium concentration of 6.1 mmol/litre on admission to ITU and a sodium concentration of 129 mmol/litre on the first postoperative day.

The patient underwent a second lavage 2 months later with 17 litres of buffered saline. He received propofol as an anaesthetic, and had an uneventful postoperative course.

## Discussion

Pulmonary alveolar proteinosis is a disease of unknown aetiology characterised by the accumulation of protein, phospholipid, cholesterol, and free fatty acid within the alveolar spaces. Du Bois *et al.* reviewed 10 years' experience of bronchoalveolar lavage to treat alveolar proteinosis in 10 patients who underwent 53 lavages.[9] The average pre-operative $Pao_2$ in their patients was 9.1 kPa on air, and they noted the lack of peri-operative problems; up to 40 litres of normal saline was used for lavage. Ventilation was required for only 2–4 hours postoperatively, and there were no cardiovascular sequelae.

The patient we have described was of similar age and fitness as those in Du Bois' review, but his postoperative recovery was very different. His prolonged stay in ITU was caused by cardiovascular instability which required invasive monitoring and inotropic support. There was no evidence of myocardial infarction or sepsis, but a degree of temporary adrenocortical insufficiency was demonstrated. His cardiovascular depression coincided with low serum cortisol concentrations and responded to cortisol replacement therapy. Owen and Spence[8] suggested that the degree of adrenocortical depression after a bolus dose of etomidate should not be harmful. In this case, administration of two boluses within a short period appears to have produced significant adverse effects.

Etomidate has many advantages when used as an induction agent and is often indicated in patients who are most at risk from adrenocortical suppression;[8] many patients in ITU require repeated anaesthesia and are likely to receive the agent more than once. We suggest that a bolus dose of etomidate may cause sufficient adrenal suppression to increase morbidity in critically ill patients, particularly if its elimination half-life is prolonged by concomitant morphine administration.[10] Serum cortisol concentration should be measured if etomidate is used for induction of anaesthesia in such patients, and if low levels coincide with cardiovascular instability, hydrocortisone replacement therapy may be of benefit. This should continue for at least 24 hours,[5] or until serum cortisol concentration is adequate without such replacement.

## References

1. Ledingham IMcA, Watt I. Influence of sedation on mortality in critically ill multiple trauma patients. *Lancet* 1983; **1:** 1270.
2. Watt I, Ledingham IMcA. Mortality amongst multiple trauma patients admitted to an intensive therapy unit. *Anaesthesia* 1984; **39:** 973–81.
3. Fraser R, Watt I, Gray CE, Ledingham IMcA, Lever AF. The effect of etomidate on adrenocortical function in dogs before and during hemorrhagic shock. *Endocrinology* 1984; **115:** 2266–70.
4. Moore RA, Allen MC, Wood PJ, Rees LH, Sear JW. Peri-operative endocrine effects of etomidate. *Anaesthesia* 1985; **40:** 124–30.
5. Wagner RL, White PF, Kan PB, Myer HR, Feldman D. Inhibition of adrenal steroidogenesis by the anesthetic etomidate. *New England Journal of Medicine* 1984; **310:** 1415–21.
6. Fry DE, Griffiths H. The inhibition by etomidate of the 11 beta-hydroxylation of cortisol. *Clinical Endocrinology* 1984; **20:** 625–9.
7. Barton RN, Little RA. Effects of inhibition of adrenal steroidogenesis on compensation of fluid loss and on survival after limb ischaemia in the rat. *Journal of Endocrinology* 1978; **76:** 293–302.
8. Owen H, Spence AA. Etomidate. *British Journal of Anaesthesia* 1984; **56:** 555–7.
9. Du Bois RM, McAllister WAC, Branthwaite MA. Alveolar proteinosis: diagnosis and treatment over a 10-year period. *Thorax* 1983; **38:** 360–3.
10. Doenicke A. Etomidate. *Lancet* 1983; **2:** 168.

*Anaesthesia*, 1989, Volume 44, pages 406–408

CASE REPORT

# Peri-operative management of severe thyrotoxicosis with esmolol

H. R. VIJAYAKUMAR, W. O. THOMAS AND J. J. FERRARA

## Summary

*A case of severe thyrotoxicosis with cardiac decompensation is reported. Use of propranolol was followed by cardiovascular collapse. Esmolol, the beta-1 adrenoceptor blocking agent was successfully used to control the thyrotoxic state. A discussion of possible advantages of esmolol is provided.*

## Key words

*Surgery*; thyroidectomy.
*Sympathetic nervous system;* beta adrenergic antagonists.

Pharmacological control of severe thyrotoxicosis has long remained a challenge despite the development of various therapeutic regimens. Lahey described the use of 'Iodin, fluids, glucose, and morphia' in 1928 for control of hyperthyroidism and to prevent the development of thyroid storm during intra-operative manipulation.[1] Thioureas and thiouracils thereafter became popular for control of the thyrotoxic patient.[2] Propranolol, a beta adrenoceptor antagonist, was introduced by Black[3] in 1964 and subsequently, after confirmation of its efficacy in a prospective study,[4] its use has become well established for control of the hyperthyoid patient before surgery.[5,6] Indeed, use of propranolol alone has been recommended as the mainstay of therapy to control hyperthyroidism prior to surgery.[7,8]

Some patients cannot be controlled by propranolol alone despite its advantages, and in some patients its use is contraindicated. The following is a case report of a patient with severe thyrotoxicosis from a toxic multinodular goitre whose clinical manifestations could not be well controlled with boluses of propranolol. The case was successfully managed by an infusion of ultrashort acting cardioselective beta blocker, esmolol.

### Case history

The patient was an 85-year-old black female admitted to the University of South Alabama Medical Center in Mobile, Alabama. For the past 50 years, she had had a slowly enlarging multinodular goitre and hypothyroidism, and had been treated with various forms of thyroid hormone replacement therapy for over 30 years. Several months before admission she was seen in an outlying clinic and placed on digoxin and frusemide for congestive heart failure. Her presenting complaints were restlessness, agitation, diarrhoea and abdominal pain; her family had noticed weakness and tremulousness, and remarked that she had eaten poorly for 2 months.

The patient's temperature on initial examination was 38°C, pulse rate 190 beats/minute and irregular, and blood pressure 170/100 mmHg. Her general appearance was that of an emaciated, frail female who had a huge bilobular goitre with each lobe measuring 9 × 12 cm. She was extremely restless and hyperreflexic.

Laboratory tests showed metabolic alkalosis, hypoxaemia, moderate leucocytosis and prerenal uraemia. The initial chest X ray showed a right lower lobe pulmonary infiltrate. An initial diagnosis of thyrotoxicosis complicated by congestive heart failure, atrial fibrillation and pneumonia was made. Thyroid function tests confirmed the clinical suspicion of thyrotoxicosis with a T3 RIA of 4.73 nmol/litre (reference range 1.54–2.93 nmol/litre), T4 RIA of 213 nmol/litre (reference range 65–155 nmol/litre), TSH of less than 0.2 mu/litre (reference range 0–5 mu/litre), and T3 RU of 0.57.

The patient was admitted to the medical intensive care unit and treatment was begun with 1.0-mg boluses of intravenous propranolol to reduce her heart rate to 110 beats/minute. She was treated with four doses of propranolol in 18 hours, followed by oral propylthiouracil

---

H.R. Vijayakumar, FFARCS, Assistant Professor, Department of Anesthesiology, W.O. Thomas, MD, Instructor, J.J. Ferrara, MD, Associate Professor, Department of Surgery, University of South Alabama, College of Medicine, 2451 Fillingim Street, Mobile, AL 36617, USA.
Correspondence should be addressed to Dr H.R. Vijayakumar please.

Accepted 4 November 1988.

0003–2409/89/050406 + 03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

200 mg every 8 hours and oral propranolol 20 mg every 8 hours. Ampicillin was begun for treatment of pneumonia.

The patient suffered an episode of circulatory collapse, within 12 hours of institution of this regimen, apnoea and bradycardia that required tracheal intubation, mechanical ventilation, atropine and adrenaline resuscitation. Inotropic support with dopamine infusion was begun to maintain haemodynamic stability, and further doses of propranolol in reduced dosage were not tolerated even with dopamine support, and therefore propranolol was discontinued. No improvement in her thyrotoxic picture was seen despite addition of intravenous sodium iodide and increasing the dose of propylthiouracil. The patient developed an ischaemic right leg, probably a consequence of femoral arterial embolisation complicating uncontrolled atrial fibrillation. She remained in an uncontrolled thyrotoxic state and her family refused surgical intervention at first.

Surgery was contemplated for failure of medical management, worsening haemodynamic status, continued ventilator dependence, increasing size of the thyroid gland and a gangrenous right leg. Invasive monitoring was established with a pulmonary artery and systemic arterial cannulation, after careful consideration of the risks of operation in an uncontrolled thyrotoxic state. A pulmonary capillary wedge pressure (PCWP) of 14 mmHg, systemic vascular resistance of 863 units and a cardiac index of 4.5 litres/minute/sq m were noted. An infusion of esmolol, the ultrashort acting beta blocker, was begun at a rate of 100 μg/kg/minute, in order to attempt pre-operative control of the thyrotoxic state. This infusion was carefully titrated to achieve a stable heart rate of 80–90 beats/minute while dopamine was used to control the arterial blood pressure. The oximetric pulmonary artery catheter showed the mixed venous oxygen saturation to be 75–78% throughout this period. Her PCWP was 12 mmHg, systemic vascular resistance 648 units and the cardiac index 4.8 litres/minute/sq m while she received esmolol and dopamine.

The patient was much more stable after 36 hours of esmolol infusion, and had no further episodes of bradycardia or hypotension. She was taken to the operating theatre after heavy sedation with diazepam where a total thyroidectomy and right above-knee amputation were performed. General anaesthesia was induced with large doses of fentanyl (33 μg/kg), vecuronium 0.1 mg/kg for muscle relaxation and midazolam 0.08 mg/kg. Her intra-operative course was uneventful and she remained stable haemodynamically throughout, despite manipulation of the large thyroid gland. Esmolol and dopamine infusions were maintained throughout surgery and continued postoperatively for 10 days, after which they were slowly withdrawn.

She required a postoperative tracheostomy for ventilatory insufficiency. Eventually, she was weaned off mechanical ventilation and was discharged temporarily to a nursing home for recuperation. She has subsequently been living at home with an above knee prosthesis.

## Discussion

Thyroid storm or crisis is characterised by a rapidly developing overwhelming exaggeration of all the manifestations of hyperthyroidism, and results in decompensation of other bodily systems.[9] A true thyroid storm probably only occurs in Graves' disease,[10] although severe hyperthyroidism from a toxic goitre can mimic this clinical picture. Our patient demonstrated clinical signs and symptoms similar to thyroid storm but the diagnosis remains essentially a clinical impression since there are no laboratory criteria to confirm it.[11,12]

The pathogenesis of thyroid storm is poorly understood.[13] The crisis may be due to a sudden release of free thyroxine[14] from its bound state or result from excessive catecholamine effects in patients who have been sensitised by excess circulating thyroid hormone.[15] Many therapeutic modalities for the management of severe thyrotoxicosis and thyroid storm have been proposed, such as spinal anaesthesia,[16] reserpine,[17] guanethidine,[18] and were historically useful for control of these difficult cases. Beta-adrenoceptor blockade with propranolol has enjoyed widespread popularity and is said to decrease the heart rate and provide symptomatic relief. However, it does not decrease cardiac output[19] or peripheral oxygen consumption.[9]

The use of propranolol alone to prepare thyrotoxic patients for operation has had good success.[5] Treatment failure and thyroid storms have been reported with this method of pre-operative preparation, despite its reported efficacy.[20–26] There are also patients in whom use of propranolol is relatively contra-indicated, such as those with brittle insulin-dependent diabetes, asthmatics and patients with congestive heart failure or heart block.[27]

It is not entirely clear why esmolol was more successful than propranolol in the control of the thyrotoxic state in our patient. It may be that the shorter half-life of this drug[28] and the nature of its administration as an infusion enabled us to titrate the beta-blockade to the required effect. It is of interest to note here that Hamilton and his colleagues[26] suggested that nadolol, which has an even longer half-life than propranolol, offers better control of the thyrotoxic state in the perioperative period.

The systemic vascular resistance was slightly lowered in our patient during the esmolol infusion. This may be due to the more selective beta-1 adrenoceptor blocking action of esmolol and the unaltered beta-2 sympathetic activity.[29] The lower systemic vascular resistance may have had a beneficial effect on the heart by reducing the afterload, and we recommend that its use be more formally evaluated in cases of severe thyrotoxicosis.

## References

1. LAHEY FH. The crisis of exophthalmic goitre. *New England Journal of Medicine* 1928; **199:** 255–7.
2. ASTWOOD EB. Treatment of hyperthyoidism with thiourea and thiouracil. *Journal of the American Medical Association* 1943; **122:** 78–81.
3. BLACK JW, CROWTHER AF, SHANKS RG, SMITH LH, DORNHORST AC. A new adrenergic beta-receptor antagonist. *Lancet* 1964; **1:** 1080–1.
4. SHANKS RG, HADDEN DR, LOWE DC, MCDEVITT DG, MONTGOMERY DAD. Controlled trial of propranolol in thyrotoxicosis. *Lancet* 1969; **1:** 993–4.
5. LEE TC, COFFEY RJ, CURRIER BM, MA X.-P, CANARY JJ. Propranolol and thyroidectomy in the treatment of thyrotoxicosis. *Annals of Surgery* 1982; **195:** 766–73.
6. TOFT AD, IRVINE WJ, SINCLAIR I, MCINTOSH D, SETH J, CAMERON EHD. Thyroid function after surgical treatment of thyrotoxicosis. *New England Journal of Medicine* 1978; **298:** 643–7.
7. ZONSZEIN J, SANTANGELO RP, MACKIN JF, LEE TC, COFFEY RJ, CANARY JJ. Propranolol therapy in thyrotoxicosis. A

review of 84 patients undergoing surgery. *American Journal of Medicine* 1979; **66:** 411–16.

8. Harrison TS. The treatment of thyroid storm. *Surgery Gynecology Obstetrics* 1965; **121:** 837.
9. Lee TC, Coffey R, Mackin J, Cobb M, Routon J, Canary J. The use of propranolol in the surgical treatment of thyrotoxic patients. *Annals of Surgery* 1973; **177:** 643–7.
10. Dobyns BM. Prevention and management of hyperthyroid storm. *World Journal of Surgery* 1978; **2:** 293–306.
11. Bartels EC. Thyroid storm or crisis. In: Werner SC, ed. *The Thyroid*, 2nd edn. New York: Harper and Row, 1962: 676–80.
12. Hamburger S, Rush D. Series on endocrine-metabolic emergencies: IV. Thyroid storm. *Journal of the American Medical Women's Association* 1981; **36:** 259–61.
13. Colebunders R, Bourdoux P, Bekaert T, Mahler C, Parizel G. Determination of free thyroid hormones and their binding proteins in a patient with severe hyperthyroidism (thyroid storm?) and thyroid encephalopathy. *Journal of Endocrinological Investigation* 1984; **7:** 379–81.
14. Lamphier T. Current status of diagnosis and treatment of thyroid storm. *Maryland State Medical Journal* 1980; **29:** 67–70.

15 Brooks MH, Waldstein SS. Free thyroxine concentrations in thyroid storm. *Annals of Internal Medicine* 1980; **93:** 694–7.

16. Knight RT. The use of spinal anesthesia to control sympathetic overactivity in hyperthyroidism. *Anesthesiology* 1945; **6:** 225–30.
17. Lővei E, Bona A. Raulwolfia serpentina and thyrotoxicosis. *British Medical Journal* 1956; **1:** 1366–7.
18. Lee WY, Bronsky D, Waldstein SS. Studies of thyroid and sympathetic nervous system interrelationships. II. Effects of guanethidine on manifestations of hyperthyroidism. *Journal of Clinical Endocrinology and Metabolism* 1962; **22:** 879–85.
19. Wilson WR, Theilen EO, Hege JH, Valenca MR. Effects of beta-adrenergic receptor blockade in normal subjects before, during, and after triiodothyronine-induced hypermetabolism. *Journal of Clinical Investigation* 1966; **45:** 1159–69.
20. Eriksson M, Rubenfeld S, Garber A, Kohler PO. Propranolol does not prevent thyroid storm. *New England Journal of Medicine* 1977; **296:** 263–5.
21. Jamison MH, Done HJ. Post-operative thyrotoxic crisis in a patient prepared for thyroidectomy with propranolol. *British Journal of Clinical Practice* 1979; **33:** 82–3.
22. Strube PJ. Thyroid storm during beta blockade. *Anaesthesia* 1984; **39:** 343–6.
23. Anaissie E, Tohmé JF. Reserpine in propranolol-resistant thyroid storm. *Archives of Internal Medicine* 1985; **145:** 2248–9.
24. Christensen PA, Nissen LR. Treatment of thyroid storm in a child with dantrolene. *British Journal of Anaesthesia* 1987; **59:** 523.
25. Feely J, Crooks J, Forrest AL, Hamilton WF, Gunn A. Propranolol in the surgical treatment of hyperthyroidism, including severely thyrotoxic patients. *British Journal of Surgery* 1981; **68:** 865–9.
26. Hamilton WFD, Forrest AL, Gunn A, Peden NR, Feely J. Beta-adrenoceptor blockade and anaesthesia for thyroidectomy. *Anaesthesia* 1984; **39:** 335–42.
27. Mackin JF, Canary JT, Pittman CS. Thyroid storm and its management. *New England Journal of Medicine* 1974; **291:** 1396–8.
28. Reilly CS, Wood M, Koshakji RP, Wood AJJ. Ultra-short-acting beta-blockade: a comparison with conventional beta-blockade. *Clinical Pharmacology and Therapeutics* 1985; **38:** 579–85.
29. Keefe DL, Somberg JC. Esmolol: a novel ultra-short-acting beta-blocking agent. *Journal of Clinical Pharmacology*. 1986; **26** (Suppl. A): A1-A2.

*Anaesthesia*, 1989, Volume 44, pages 409–411

CASE REPORT

# Hypertrophic obstructive cardiomyopathy in combination with a prolapsing mitral valve

## Anaesthesia for surgical correction with propofol

M. D. BELL AND C. S. GOODCHILD

### Summary

*The anaesthetic management of a 27-year-old woman who presented for surgical correction of hypertrophic obstructive cardiomyopathy and mitral valve prolapse is described. The rationale for using propofol in a total intravenous anaesthetic technique is discussed.*

### Key words

*Anaesthetics, intravenous*; propofol.
*Surgery*; cardiovascular.

Hypertrophic obstructive cardiomyopathy (HOCM) is one of three groups of primary cardiomyopathies; the others are idiopathic dilated, and restrictive. It is inherited as an autosomal dominant with a high degree of penetrance[1] and is associated with phaeochromocytoma and neurofibromatosis. The condition is rare and reports of incidence vary, possibly because only the obstructive subgroup presents for corrective surgery. Patients more usually present for noncardiac surgery or for cardiac investigation.

Pathologically, HOCM is characterised by an asymmetrical septal hypertrophy that consists of disorganised myocardial fibres, a small ventricular cavity and a thickened mitral valve with secondary atrial dilatation. All these features may be attributable to a primary disorder of catecholamine response or to an abnormality of calcium transport. The functional result is poor ventricular compliance and filling and, as in this case, outflow obstruction with mitral regurgitation. One hypothesis for the obstruction is that it causes an exaggerated anterior motion of the anterior mitral valve leaflet during systole.[2] Presenting symptoms are chest pain and dyspnoea, palpitations and syncope. The high incidence of arrhythmias leads to sudden death in many patients[3] and it is the most common postmortem finding in athletes dying during physical exercise. The presence of mitral regurgitation increases the incidence and severity of dyspnoea on exertion.

Signs include the systolic murmur of aortic obstruction and of mitral regurgitation with or without a thrill. The electrocardiogram (ECG) reveals changes of left ventricular hypertrophy and strain with atrial enlargement. Ambulatory monitoring usually reveals arrhythmias, particularly ventricular ectopic beats, which are easily evoked by a minimum of exertion.

We describe here a patient with the typical features of HOCM undergoing open-heart surgery. A total intravenous anaesthetic technique with propofol and diamorphine was used.

### Case history

A 27-year-old female presented to the cardiology clinic in December 1986 for investigation of a murmur first diagnosed in 1980 during her first pregnancy. She complained of attacks of palpitations that lasted around 20 minutes and increasing shortness of breath. She had no other symptoms, but did suffer from nocturnal epilepsy controlled for the last 16 years by phenytoin 150 mg nocte. She was obese, had a resting arterial blood pressure of 106/56 mmHg, and her heart rate was 56 beats/minute, sinus rhythm. Her chest X ray showed left ventricular hypertrophy confirmed by ECG, which also revealed strain. An echocardiogram showed HOCM; she was advised to stop smoking and treatment with verapamil 80 mg three times a day was started.

Catheter studies in August 1987 revealed a gradient of 30 mmHg across the aortic valve, a left ventricular end diastolic pressure of 25 mmHg and severe mitral regurgitation. She was scheduled for mitral valve replacement and excision of ventricular muscle in November 1987.

---

M.D. Bell, FFARCS, Senior Registrar, C.S. Goodchild, PhD, FFARCS, Lecturer and Honorary Consultant, The General Infirmary at Leeds and the University of Leeds Department of Anaesthesia, Leeds LS2 9LN.

Accepted 21 November 1988

0003–2409/89/050409 + 03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

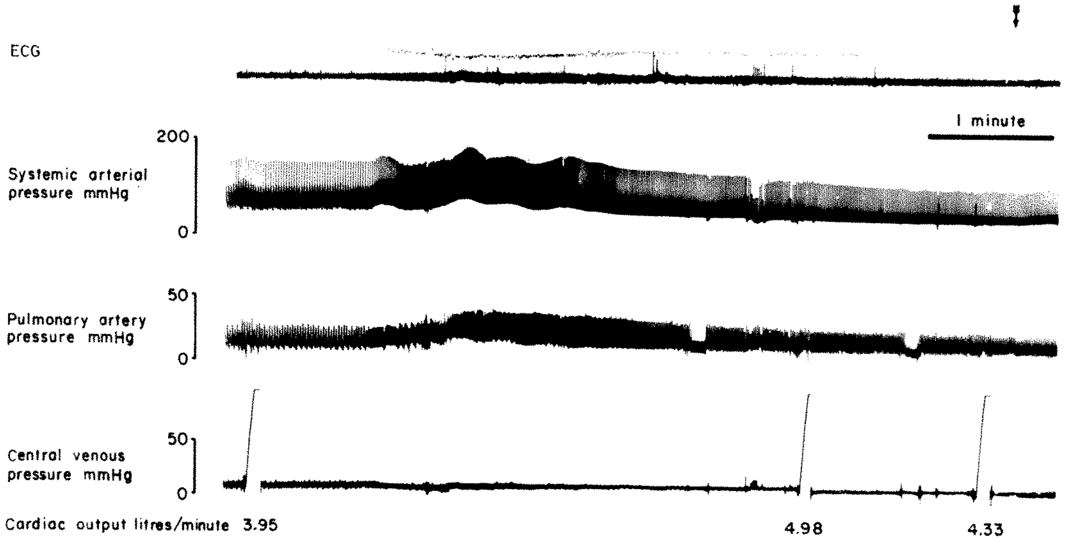


**Fig. 1.** Cardiovascular changes during induction of anaesthesia with propofol 1 mg/kg over 4 minutes.

### *Procedure*

The patient was premedicated with papaveretum 10 mg and hyoscine 0.2 mg 2 hours before operation. On arrival in the operating theatre, using local anaesthesia, an intravenous infusion was established, an arterial line inserted in the left radial artery and a pulmonary artery thermodilution catheter inserted via the right internal jugular vein.

Baseline readings were as follows: heart rate 60 beats/minute; systemic arterial pressure 105/50 mmHg; central venous pressure 14 mmHg; pulmonary artery pressure 26/8 mmHg; pulmonary artery occlusion pressure 9 mmHg; cardiac output 3.95 litres/minute. After pre-oxygenation, anaesthesia was induced with diamorphine 12 mg, pancuronium 12 mg and propofol 80 mg delivered by a volumetric infusion pump in 4 minutes.

An initial tachycardia of 110 beats/minute decreased to a resting level of 60 beats/minute by 5 minutes, associated with an increase of arterial pressure to 170/100 mmHg followed by a decrease to 105/35 mmHg at 5 minutes after induction. Pulmonary artery pressure increased to 40/20 mmHg when artificial ventilation by mask was instituted, and decreased to 23/8 mmHg with the pulmonary artery occlusion pressure down to 8 from a high of 18 mmHg. Central venous pressure gradually fell to 4 mmHg. Cardiac output was 5.0 litres/minute at 3 minutes and 4.3 litres/minute at 5 minutes after induction. Tracheal intubation at 5 minutes resulted in no cardiovascular changes other than a slight rise in arterial pressure to 118/35 mmHg. The lungs were ventilated with air and oxygen ($F\text{IO}_2$ 0.5) at a rate of 14 breaths/minute and tidal volume of 8 ml/kg to achieve normocapnia. Insertion of a nasogastric tube at 7 minutes, however, resulted in a further increase in arterial pressure to 155/66 mmHg with no change in the other parameters. This was treated with a bolus of 5 mg of propofol followed by an infusion at a rate of 480 mg/hour (6 mg/kg/hour).

All cardiovascular variables remained stable and surgery started at 16 minutes after induction. The arterial blood pressure increased in response to skin incision to 185/80 mmHg and was treated by a bolus of 20 mg propofol and an increase in the infusion rate to 680 mg/hour. Further increments of 4 mg diamorphine and 20 mg propofol and an infusion rate of 780 mg/hour controlled the arterial pressure at 145/60 mmHg. Sternotomy subsequent to this produced a further increase of only 10 mmHg and all other cardiovascular variables remained stable until cardiopulmonary bypass was established at 1 hour after induction; at this point the propofol infusion rate was reduced to 480 mg/hour. Diamorphine 10 mg was added to the pump prime. One litre of compound sodium lactate solution and 500 ml of hydroxyethyl starch were administered before bypass, and 500 ml of urine were produced. The propofol infusion was turned off once the patient was cooled to 29°C. Excision of ventricular muscle below the aortic valve and replacement of the abnormal mitral valve were performed uneventfully.

Eighty milligrams of propofol followed by an infusion of 240 mg/hour was administered once she was rewarmed to 37°C. Three attempts at defibrillation were necessary, with the addition of 100 mg lignocaine.

The cardiovascular variables immediately after bypass were: heart rate 76 beats/minute (sinus rhythm); arterial blood pressure 105/35 mmHg; central venous pressure 8 mmHg; pulmonary artery pressure 35/16 mmHg; pulmonary artery occlusion pressure 18 mmHg; cardiac output 3.9 litres/minute.

There was no cardiovascular change on slow administration of protamine and all readings remained stable for the next hour, during which surgery was completed. The patient was transferred to the intensive care unit and her lungs ventilated. The infusion of propofol at 240 mg/hour was continued for 2.5 hours. She was alert, cooperative, pain free and breathing spontaneously with stable cardiovascular variables at 3 hours after surgery (i.e. 30 minutes after the end of the propofol infusion). No evidence of epileptiform activity had appeared on a cerebral function analysing monitor. Her trachea was extubated at that time, she was discharged to the surgical ward the next morning and from the hospital on day 8. On review at the clinic 3 and 6 months later she was asymptomatic with no adverse sequelae.

## Discussion

The conduct of anaesthesia for HOCM relates to the knowledge that this disease is a dynamic phenomenon, with catecholamine surges that aggravate any obstruction. Optimum output is achieved by optimising filling pressure, and by controlling the heart rate in sinus rhythm the atrial contribution to ventricular filling approaches 75% of total stroke volume.[4] Arrhythmias require prompt treatment. Preservation of an adequate perfusion pressure and systemic vascular resistance should revolve round the use of vasoconstrictors rather than inotropes which may increase the outflow obstruction. A perfect anaesthetic induction is smooth and maintains filling pressures and peripheral resistance. It is obvious that no anaesthetic agent reaches this ideal.

There is little in recent literature about anaesthesia for HOCM. The use of propofol in cardiac surgery has been principally in the context of coronary artery grafting, where it is hard to dissociate the primary disease and the related therapy of $\beta$ blockers and calcium antagonists from the cardiovascular effects of propofol.[5] Literature about its usage in valve surgery relates to the previous formulation in Cremophor.[6] There do not seem to be any accounts on the use of propofol for anaesthesia for HOCM. Studies on its use as an induction agent for noncardiac surgery[7] suggest that a modest decrease or no change in heart rate are to be expected, a point in its favour. On the negative side, however, systemic vascular resistance and venous return would both be expected to decrease; both effects are potentially deleterious in a patient with HOCM.

Venodilatation with increase in capacitance and arteriolar vasodilatation occur with all modern anaesthetic agents, because of their central nervous system depressant action on decreasing sympathetic nervous system tone. In addition, however, propofol exerts a direct relaxant effect on the smooth muscle of veins, and thus produces further falls in central venous pressure and pulmonary artery occlusion pressure (personal observations). The problem is easily countered by slight elevation of the legs and infusion of colloid as induction proceeds. This is our routine during cardiac anaesthesia and we find, as in this case, that cardiac output and arterial blood pressure are well maintained. We conclude therefore that the cardiovascular profile of propofol is compatible with the management of cases of HOCM.

## References

1. Wynne J, Braumwald E. *Cardiomyopathies and myocarditis.* Philadelphia: Saunders and Co., 1984.
2. Henry WL, Clarke CE, Glancy DL, Epstein SE. Echocardiographic measurements of left ventricular outflow gradient in idiopathic hypertrophic subaortic stenosis. *New England Journal of Medicine* 1973; **288:** 989–93.
3. Maron BJ, Roberts WC, Edward JE, McAllister HA, Foley DD, Epstein SE. Sudden death in patients with hypertrophic obstructive cardiomyopathy: characteristics of 26 patients with functional limitations. *Annals of Cardiology* 1978; **41:** 803.
4. Hanrath P, Mathey DG, Kremer B, Sontag F, Bleifeld W. Effect of verapamil on left ventricular isovolumic relaxation time and regional left ventricular filling in hypertrophic obstructive cardiomyopathy. *American Journal of Cardiology* 1980; **45:** 1258.
5. Stephan H, Sonntag HO, Schenck D, Kettler D, Khambatta HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease. *British Journal of Anaesthesia* 1986; **58:** 969–75.
6. Aun C, Major E. The cardiorespiratory effect of ICI 35868 in patients with valvular heart disease. *Anaesthesia* 1984; **39:** 1096–1100.
7. Ground RM, Twigley AJ, Carli F, Whitwam JG, Morgan M. The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. *Anaesthesia* 1985; **40:** 735–40.

*Anaesthesia*, 1989, Volume 44, pages 412–414

APPARATUS

# The oesophageal detector device

## A prospective trial on 100 patients

K. N. WILLIAMS AND J. F. NUNN

**Summary**

*Misplacement of a tracheal tube in the oesophagus remains a significant cause of mortality and morbidity in anaesthesia, despite decades of effort aimed at prevention, or perhaps more importantly, detection, of such an event. We have evaluated a cheap, simple and quick device which relies mainly on the reflation or otherwise of an Ellick's evacuator applied to the supposed 'tracheal' tube. Identical tracheal tubes were passed into the trachea and oesophagus of 100 patients; the left and right position in the mouth was chosen at random. The test was conducted by a second anaesthetist, not present at intubation, and unaware of which tube was in the trachea. There were no false positive results and the correct deduction of which was the tracheal tube was reached in 100 tests using this device. Its use is recommended for widespread evaluation as a valuable adjunct to existing methods of detecting misplacement.*

**Key words**

*Intubation, tracheal*; complications.
*Equipment*; oesophageal detector device.

Misplacement of the tracheal tube in the oesophagus remains a significant cause of mortality and morbidity in anaesthesia, despite decades of work. Many ways to prevent it have been advocated, but early detection of misplacement is perhaps even more important. The clinical signs of correct placement are, unfortunately, all fallible, albeit infrequently. These signs include chest expansion on inflation, apical chest expansion, auscultation at the lung apices, abdominal distension, and detection of airflow on compression of the chest. Most anaesthetists in this country use a combination of the above to confirm correct placement. Detection of expired $CO_2$ is popular in America and elsewhere. Many maintain, however, that the *only* reliable sign of correct placement is visualisation of the tube between the vocal cords.

Wee[1] described a test which relies upon the relative rigidity of the tracheal wall, as compared to that of the oesophagus. The latter will collapse over the end of a rigid tube when a negative pressure is applied to it and thus prevent the aspiration of air which occurs freely from the more rigid trachea. Nunn[2] simplified Wee's device so that it could be used single-handed and even more quickly. He suggested the use of an Ellick's evacuator bulb attached to a tracheal tube connector, either Portex or Nosworthy. This device first inflates the viscus and this inflation, when the tube is in the oesophagus, is often accompanied by a characteristic flatus-like noise, followed by absent or markedly delayed refilling. In contrast, the inflation of a tube in the trachea is silent and the refill instantaneous.

Such a device can be recommended only if it is shown to be reliable, and we now describe results obtained prospectively from 100 patients.

## Methods

Ethics Committee approval was obtained to pass a second tracheal tube into the oesophagus and to use the device on 100 patients who had surgery at Northwick Park Hospital and for whom tracheal intubation was clinically indicated. All anaesthetists at the hospital cooperated in this prospective study.

The patients were anaesthetised, their tracheas intubated in the normal fashion and correct placement of the tracheal tube was confirmed by conventional means. The tracheal tube was then moved to the right side of the patient's mouth, as viewed from the vertex if, after intubation, the second hand of the anaesthetic room wall clock was between 1 and 30 seconds, or to the left if between 31 and 60 seconds. A second, identical tracheal tube was then placed in the oesophagus and the cuff inflated; the patient's lungs were pre-oxygenated before the detector device was tested. The patient was then

---

K.N. Williams, MA, MB, BS, FFARCS, Senior Registrar, Department of Anaesthetics, J.F. Nunn, PhD, MD, FRCS, FFARCS, FFARACS (Hon), FFARCSI (Hon), Head of CRC Division of Anaesthesia, Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ.

Accepted 4 November 1988.

0003–2409/89/050412 + 03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

disconnected from the ventilator and a second, waiting anaesthetist called into the anaesthetic room to use the device on each tube in turn. He noted any noise on inflation, and graded the speed of reflation as instant, delayed or none. The assessor repeated the test if necessary until he was satisfied which tube was in the trachea. The 'intubating' anaesthetist then reconnected the patient to the ventilator and proceeded to surgery. Documentation included any comments, the variety of tube and connector, which side of the mouth the tracheal tube was sited and a reason if the test was inconclusive at the first attempt.

## Results

There were 31 males (mean age 62.0 years, range 24–84) and 69 females (mean age 47.6 years, range 16–90) in the study. The preponderance of females was due to the high frequency of intubations in gynaecology for laparoscopy, and this also accounts for their relative youth. The varieties of tracheal tube employed (Table 1) reflects clinical indications for specific tubes and the personal preference of the participating anaesthetists.

No test was regarded as inconclusive and the assessor's determination of which tube was in the trachea was correct in every case (Table 2). The presence of the flatus sound on inflation was present on 87% of occasions with oesophageal tubes, but consistently absent with tracheal tubes.

The tracheal tube was slow to refill on two occasions; both times the tubes had the usual Magill side-facing bevel, but there was still never any doubt of tracheal placement. The oesophageal tube permitted incomplete refilling of the Ellick's bulb on 16 occasions and on two occasions refilling was reasonably rapid, though not sufficient to mimic tracheal placement.

Slow reflation from oesophageal tubes occurred more frequently with rubber tubes than with Portex (Table 1), and this difference is significant at the 1% level by the Chi-squared test and either variant of Fisher's exact test. This difference might be explained either by the relative rigidity of Portex tubes or by the presence of an external pilot channel on the rubber tubes.

**Table 1.** Tracheal tubes employed.

| | Portex | Red rubber Magill | Oxford | Reinforced Latex |
|---|---|---|---|---|
| Total | 79 | 13 | 5 | 3 |
| Slow refill from | | | | |
| Trachea | 2 | 0 | 0 | 0 |
| Oesophagus | 7 | 5 | 1 | 3 |
| Tracheal tube | | | | |
| Left-sided | 31 | 3 | 0 | 1 |
| Right-sided | 48 | 10 | 5 | 2 |

**Table 2.** Assessors response.

| | Tracheal tube | Oesophageal tube |
|---|---|---|
| *Observations* | | |
| Silent inflation | 100 | 13 |
| Noisy inflation | 0 | 87 |
| Instantaneous refill | 98 | 0 |
| Delayed refill | 2 | 16 |
| No refill | 0 | 84 |
| Number of multiple attempts | 1 | |
| *The decision* | | |
| Tracheal placement | 100 | 0 |
| Oesophageal placement | 0 | 100 |

The assessor twice required a second attempt to come to a decision during a pilot trial on 20 patients, and on both occasions the second test resulted in slow refilling of the oesophageal tube. One repeat was required during the study period and oesophageal refilling was absent on the second attempt.

## Discussion

This device is cheap, simple, and convenient to operate single-handed and in less than 5 seconds; its components are available in most operating theatres. Instant refilling appears to be a reliable predictor of correct placement. There may be confusion if an oesophageal tube is tested more than once, since subsequent inflations may be silent and refilling may occur, but it is always delayed and incomplete. We ascribe this to the aspiration, on the second attempt, of air instilled during the first.

Delayed, though complete, refilling *may* occur with tracheal placement, though the rate of refilling is qualitatively faster and more complete than that observed after repeated oesophageal inflation. This has only occurred with tubes that have a side-facing bevel and may therefore be the result of partial mucosal occlusion of the tube's orifice.

The device may also have a place at surgical tracheostomy since paratracheal or submucosal intubation could have serious consequences.[3] The device should be applied *deflated* in such circumstances and the rate of refilling alone used as the guide to correct placement. This is because preliminary inflation of a submucosal tube runs the theoretical risk of mucosal dissection and irretrievable airway obstruction. A similar indication exists for the increasingly popular practice of minitracheostomy, which may also be hazardous.[4] These devices may easily be tested with the size 4.0 Portex connector supplied as an intermediate connector (Fig. 1).

The speed of use with this detector makes it ideal for testing tubes placed by the blind nasal technique, particularly if this method has been chosen after failure to intubate by conventional laryngoscopy. It has been suggested that the device may further be refined to include a colorimetric $CO_2$ analyser (similar to a breathalyser) in series with the evacuator, which would thus provide a chemical as well as a physical indicator of correct placement. This would however add to the cost and complexity of the device.

The incidence of false positive and negative results, although zero in a trial of only 100 patients, implies confidence limits of at most 6%. Tighter confidence limits can be achieved only with a larger series, for example 1000 correct tests would give an upper limit of only 0.6%. Clearly the device now requires evaluation on a much larger scale.

## Note added in proof

Since this paper was submitted, O'Leary and his colleagues have published a trial of 25 tracheal and 25 oesophageal intubations using a method based on the aspiration

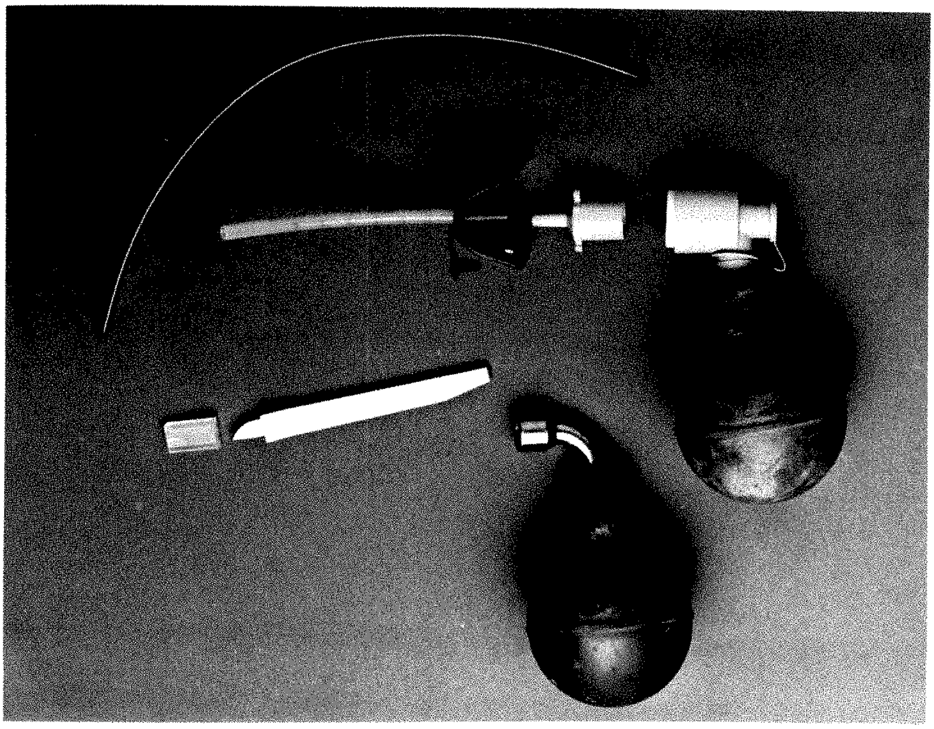


**Fig. 1.** The oesophageal detector device shown with a connector to attach it to a minitracheostomy tube. The device is also shown with a Nosworthy adaptor.

of 30 ml air into a syringe.[5] Their test correctly distinguished tracheal and oesophageal intubation in every case. They emphasise the importance of aspirating with the cuff deflated so as to avoid alveolar collapse; since our device first instils some 50 ml air before re-aspirating, we are prepared to use it with the cuff inflated, which further simplifies its operation.

## Acknowledgments

We are grateful to all anaesthetists at Northwick Park Hospital who have helped in the study. Dr R.S. Cormack gave valuable help with the statistical evaluation.

## References

1. Wee MYK. The oesophageal detector device. Assessment of a new method to distinguish oesophageal from tracheal intubation. *Anaesthesia* 1988; **43:** 27–9.
2. Nunn JF. The oesophageal detector device. *Anaesthesia* 1988; **43:** 804.
3. Wright MM. Shearer AJ. Tracheostomy tube insertion and replacement *Anaesthesia* 1984; **39:** 717–8.
4. Tran Y. Hedley R. Misplacement of a mini-tracheotomy tube. *Anaesthesia* 1987; **42:** 783.
5. O'Leary JJ, Pollard BJ, Ryan MJ. A method of detecting oesophageal intubation or confirming tracheal intubation. *Anaesthesia and Intensive Care* 1988; **16:** 299–301.

*Anaesthesia*, 1989, Volume 44, pages 415–418

APPARATUS

# Fluid flow through dural puncture sites

## An *in vitro* comparison of needle point types

R. H. CRUICKSHANK AND J. M. HOPKINSON

## Summary

*Leakage of artificial cerebrospinal fluid through human dura was measured in vitro after puncture by spinal needles. Fluid loss tailed off in all cases and ceased within 5 minutes in 10% of punctures made with a 22-gauge needle, 28% made with a 26-gauge and 65% made with a 29-gauge needle ($p < 0.05$). The fluid loss was not reduced by alignment of the bevel of the needle parallel to the longitudinal direction of the fibres. Whitacre point needles of 22 gauge produced lower fluid loss than a 22-gauge Quincke point needle inserted across the fibres ($p < 0.05$). Leakage rate was related to needle size, but not related to the alignment of a Quincke point. Little or no leakage occurred with 29-gauge needles.*

## Key words

*Anaesthetic techniques, regional*; spinal.
*Equipment*.

The use of intrathecal anaesthesia has been limited by postspinal headache due to cerebrospinal fluid (CSF) loss through the puncture site. The incidence has been reduced to less than 1% with the introduction of fine-gauge 0.5 mm (25-gauge) and 0.45 mm (26-gauge) needles.[1] Recently, even finer gauge needles (26-gauge and smaller) have become available in an attempt further to reduce this complication.

In 1926, Greene[2] demonstrated that CSF loss after dural puncture was greater with a 19-gauge than with a 22-gauge needle. He postulated that insertion of the spinal needle point parallel to the direction of the longitudinal fibres of the dura, separated rather than cut the fibres as would occur with the bevel aligned across the fibres. This study has not been repeated with the smaller needles now available. *In vivo* studies on alignment of the needle bevel suggest that to puncture the dura with the needle bevel parallel to the direction of the dural fibres may be more important than needle size.[3] Pencil point needles also have a theoretical advantage in reducing damage to the dural fibres.[4]

The aim of the present study was to produce a model of dural puncture to assess if apparent differences in CSF leakage in relation to needle size, type and alignment could be quantified and also to assess the performance of a new 29-gauge needle. A pilot study that used animal dura and saline had showed that there was no apparent difference in point alignment and that the fluid loss tailed off rapidly. This study used human dura and artificial CSF.

## Methods

Fresh human postmortem thoracolumbar spinal dura mater, provided by the neuropathology department at the Royal Hallamshire Hospital, was studied. Portions were mounted so that the longitudinal axis of the specimen ran vertically in a purpose-built brass jig with a 1-cm diameter porthole. The dura was fixed across the porthole and clamped in place between the two halves of the apparatus with a rubber 'O' ring to produce a watertight seal (Fig. 1).

The dura was then connected to a reservoir system filled with an artificial CSF of similar biochemical constitution, viscosity and density to real CSF. It was made up from the formulation used in previous studies of CSF flow through spinal needles.[5] This system was adjusted to produce a pressure of 12 cm of CSF behind the dura to mimic the physiological pressure of CSF whilst lying. Samples were discarded when it was impossible to obtain a sealed system.

Spinal needles of 22 gauge (0.7 mm), 26 gauge (0.45 mm) and 29 gauge (0.34 mm) of various makes were studied (Table 1). The external diameter of each needle was measured to confirm that those used were of equivalent size. For each size of Quincke needle, a comparison was made between punctures with the bevel parallel to and across the longitudinal fibres of the dura. In the 22- and 26-

---

R.H. Cruickshank,* FFARCS, Lecturer, J.M. Hopkinson, MB, ChB, Senior House Officer, Department of Anaesthetics, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2 JF.
* Present appointment: Senior Registrar in Anaesthetics, Leeds General Infirmary, Great George St, Leeds LS1 3EX.
Accepted 5 December 1988.

0003–2409/89/050415 + 04 $03.00/0
© 1989 The Association of Anaesthetists of Gt Britain and Ireland

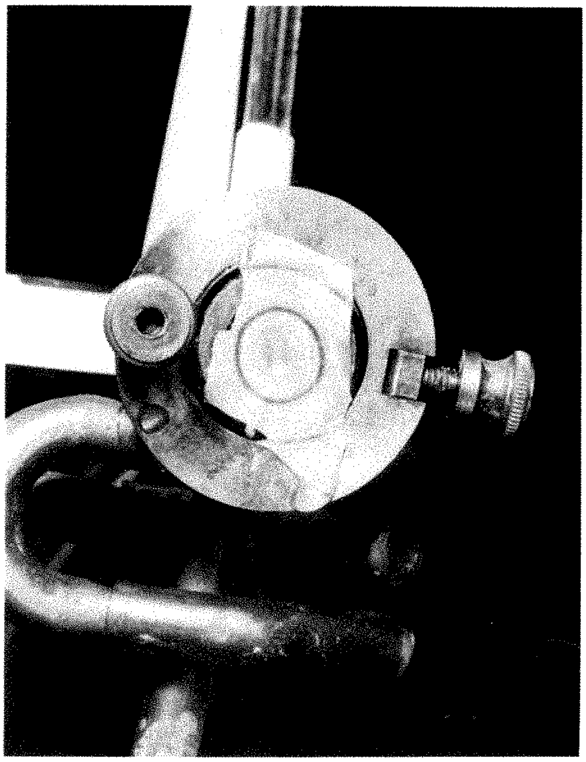


**Fig. 1.** Dura mounted across the porthole of the apparatus.

**Table 1.** Needles studied.

| | External diameter (mm) |
|---|---|
| 22-gauge Quincke point Becton Dickinson (BD) | 0.5 |
| 22-gauge Whitacre point (Monoject) | 0.5 |
| 26-gauge Quincke point (Vygon) | 0.45 |
| 26-gauge Greene point (BD) | 0.45 |
| 29-gauge Quincke point (Vygon) | 0.34 |

gauge studies, equivalent size needles with pencil point type needles were also assessed (Fig. 2).

**Table 2.** Time to appearance of CSF at needle hub. Seconds, mean (range).

| | CSF pressure 1.2 kPa | CSF pressure 5.0 kPa |
|---|---|---|
| 22 gauge (BD) | 2.3 (1.5–5) | 1 (1) |
| 26 gauge (Vygon) | 9.0 (8–15) | 2.3 (2–3) |
| 29 gauge (Vygon) | 42.2 (28–61) | 8.4 (6–10) |

A spinal needle was selected at random and a single puncture made. The needle was removed immediately and a clock started. CSF pressure was kept at 1.2 kPa, with small adjustments in the reservoir height if necessary. Any fluid which leaked from the puncture site was collected for 5 minutes and measured gravimetrically. Holes were made with the bevel longitudinal to the fibres, the bevel across the fibres or with an equivalent size pencil point. Twenty holes were made with each needle size and in each alignment of the needle point. Five examples of each needle were used.

On the first occasion each Quincke point needle was used, the time to appearance of CSF at the hub was determined at CSF pressures of 1.2 and 5 kPa as part of the study.

Statistical analysis used nonparametric analysis of variance and Mann–Whitney *U* tests. Chi-squared and Fisher's exact tests were used to compare the incidence of cessation of leakage. Statistical significance was accepted at the 5% value.

## Results

Time to appearance of CSF at the needle hub is shown in Table 2. This was difficult to assess in the 29-gauge needles, which have an opaque hub. It took up to 61 seconds for CSF to appear at 1.2 kPa pressure, which may make identification of correct placement in clinical use difficult. CSF appeared much more rapidly at 5.0 kPa, with a mean time of 8 seconds.

Volumetric loss through the holes in the first 5 minutes is shown in Table 3. There was no significant difference in fluid loss between bevel alignments or needle point types

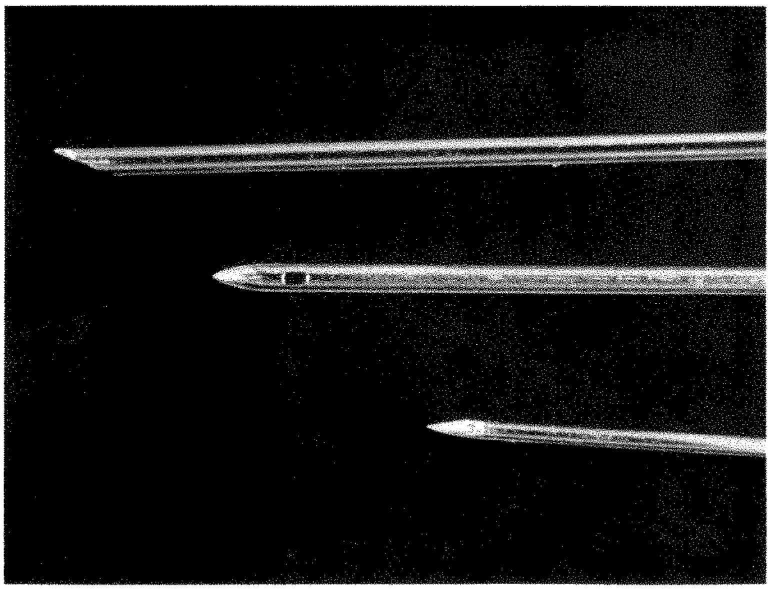


**Fig. 2.** *Top:* 22-gauge Quincke point; *middle:* 22-gauge Whitacre point (pencil point); *lower:* 26-gauge Greene point.

**Table 3.** Total CSF loss through puncture sites over a 5-minute period; median (range).

| | | Number of punctures | Median volume (ml) | |
|---|---|---|---|---|
| 22-gauge Quincke | Parallel | 20 | 5.88 | (0.6–26.7) |
| | Across | 20 | 8.55 | (2.3–26.6) |
| 22-gauge Whitacre | | 20 | 4.64 | (0.0–24.1)* |
| 26-gauge Quincke | Parallel | 20 | 0.94 | (0.0–7.32) |
| | Across | 20 | 1.20 | (0.0–8.05) |
| 26-gauge Greene | | 20 | 1.77 | (0.0–8.22) |
| 29-gauge Quincke | Parallel | 20 | 0.03 | (0.0–3.29) |
| | Across | 20 | 0.09 | (0.0–2.67) |

* $p < 0.05$ compared with 22-gauge across; all 26-gauge $p < 0.01$ compared with 22-gauge; all 29-gauge $p < 0.01$ compared with 26-gauge.

**Table 4.** CSF loss (ml/minute) after 5 minutes.

| | | Number of punctures | Median flow rate | Range |
|---|---|---|---|---|
| 22-gauge Quincke | Parallel | 20 | 0.52 | (0.0–5.01) |
| | Across | 20 | 1.32 | (0.1–5.12) |
| 22-gauge Whitacre | | 20 | 0.59 | (0.0–4.04) |
| 26-gauge Quincke | Parallel | 20 | 0.04 | (0.0–1.24) |
| | Across | 20 | 0.12 | (0.0–1.50) |
| 26-gauge Greene | | 20 | 0.24 | (0.0–1.52) |
| 29-gauge Quincke | Parallel | 20 | 0.00 | (0.0–0.75) |
| | Across | 20 | 0.00 | (0.0–2.53) |

All 26-gauge $p < 0.01$ compared with all 22-gauge; all 29-gauge $p < 0.01$ compared with all 26-gauge.

**Table 5.** Number of punctures not leaking

| | | Number of punctures | Initially | By 5 minutes |
|---|---|---|---|---|
| 22-gauge Quincke | Parallel | 20 | 0 | 3 |
| | Across | 20 | 0 | 0 |
| 22-gauge Whitacre | | 20 | 1 | 3 |
| 26-gauge Quincke | Parallel | 20 | 4 | 9 |
| | Across | 20 | 2 | 5 |
| 26-gauge Greene | | 20 | 1 | 3 |
| 29-gauge Quincke | Parallel | 20 | 8 | 13 |
| | Across | 20 | 8 | 13 |

All 26-gauge $p < 0.05$ compared with 22-gauge at 5 minutes; all 29 gauge $p < 0.01$ compared with 26-gauge at 5 minutes; 26-gauge Greene $p < 0.05$ compared with 26-gauge parallel at 5 minutes.

within each needle size, except in the 22-gauge group, where the loss from Whitacre (pencil) point punctures was less than from the Quincke bevel aligned across the fibres.

CSF loss rate after 5 minutes is shown in Table 4. Loss rate was related to needle size but not to the type of point. Six out of a total of 60 holes (10%) made with a 22-gauge needle had stopped leaking, compared with 17 out of 60 holes (28%) made with a 26-gauge needle. Twenty six of the 40 holes (65%) made with a 29-gauge needle had stopped leaking (Table 5).

There was a decline in flow over the 5 minutes of between 3% and 100% of the initial flow in all cases, which indicated some recoil of the dural fibres. However, this decrease in flow did not occur if a nonfibrous plastic membrane was substituted for the dura.

## Discussion

This study suggests that needle size is of major importance in the reduction of fluid leakage from dural puncture sites, but it does not support the view that longitudinal puncture incisions reduce initial fluid leakage, although median flow rates were lower. There was no apparent advantage in using pencil points. The 29-gauge needles produced little or no dural leak, but may be difficult to use clinically since appearance of CSF may take over a minute whilst the patient is lying down.

The alignment of the needle point has only rarely been commented on in studies of the incidence of postspinal headache, but one study that used 22- and 25-gauge needles suggested that needle point alignment was more important than the needle size.[3]

Hart and Whitacre[6] advocated the use of a pencil point needle without a cutting edge to reduce trauma to the dural fibres. They claimed a decrease in incidence of headache from 5% to 2% using 20-gauge needles with a pencil point. Haraldson[7] noted a decrease of headache from 32% to 9% using noncutting needles in obstetric patients. Quincke point needles remain in widespread use despite these studies. Twenty-two-gauge pencil points produced less leakage in the present study than an equivalent size Quincke point inserted across the fibres. Pencil points produced higher median fluid loss in the 26-gauge study, although this was not statistically significant. Significantly fewer pencil point holes stopped leaking in this group compared with punctures made with Quincke needles with the bevels parallel to the dural punctures.

The potential for CSF leakage in the larger needle sizes is very great and the epidural space must play a significant role in the reduction of this leak. Franksson *et al.*[8] demonstrated that the epidural space could accommodate a leakage of only 0.17 ml/minute at normal CSF pressures. They also noted that the holes made by 0.5-mm and 1-mm Quincke pointed needles were crescent shaped and they demonstrated that a puncture made with the bevel across the longitudinal fibres tore off about twice as many of these fibres.

The hole was inspected after each puncture in our study. Those made by Quincke needles with the bevel longitudinal to the fibres were frequently 'v' or crescent shaped and had not separated the predominantly longitudinal fibres; this left a free flap of dura, as described by Dittman *et al.*[9] The widely held belief that longitudinal punctures split the dural fibres seems to be an over simplification.

In conclusion, while this study could not demonstrate the apparent advantage of aligning the bevel of the needles parallel to the direction of the fibres *in vivo*, it appears that a reduction of fluid loss of greater magnitude can be achieved by the use of smaller needles. Provided that a single puncture can be made, the introduction of even smaller needles should further reduce the incidence of postspinal headache.

## Acknowledgments

We are grateful to Dr C. H. L. Smith, neuropathologist, for samples of dura, Dr J. D. Alderson, for help and advice, Mr D. Wortley, for constructing the equipment and Mr T. Moore, Principal Pharmacist, for formulating the artificial CSF.

## References

1. BONICA JJ. Postspinal Complications. In: SHNIDER SL, ed. *Obstetrical anesthesia. Current concepts and practice.* Baltimore: Williams and Wilkins, 1970: 174–80.

2. Greene HM. Lumbar puncture and the prevention of postpuncture headache. *Journal of the American Medical Association* 1926; **86:** 391–2.
3. Mihic DN. Postspinal headache and relationship to the longitudinal dural fibres. *Regional Anesthesia* 1985; **10:** 76–81.
4. Moore DC. *Regional block*, 4th edn. Springfield, Illinois: Charles C. Thomas, 1965: 358–9.
5. Gerrish SP, Peacock JE. Variations in the flow of cerebrospinal fluid through spinal needles. *British Journal of Anaesthesia* 1987; **59:** 1465–71.
6. Hart JR, Whitacre RJ. Pencil-point needle in prevention of postspinal headache. *Journal of the American Medical Association* 1951; **147:** 657–8.
7. Haraldson S. Headache after spinal anesthesia: experiments with a new spinal needle. *Anesthesiology* 1951; **12:** 321–7.
8. Frankson C, Gordh T. Headache after spinal puncture and a technique for lessening its frequency. *Acta Chirugica Scandinavica* 1951; **94:** 443–54.
9. Dittmann M, Schafer HG, Ulrich J, Bond-taylor W. Anatomical re-evaluation of lumbar dura mater with regard to postspinal headache. Effect of dural puncture. *Anaesthesia* 1988; **43:** 635–7.

*Anaesthesia*, 1989, Volume 44, pages 419–424

APPARATUS

# The pneuPAC ventilator with new patient valve and air compressors

G. R. PARK, A. R. MANARA, A.R. BODENHAM AND C. J. MOSS

## Summary

*The pneuPAC Model 2-R pneumatic logic ventilator with a new air entrainment valve that offers the option of an* $F\text{IO}_2$ *of 1.0 or 0.45 is described. Its robustness, portability, variable* $F\text{IO}_2$*, choice of positive end expiratory pressure and pressure relief valves make it versatile and suitable for transporting critically ill patients, as well as for resuscitation use when adverse conditions may be encountered. Two new medical air compressors, one mains driven and the other battery powered, designed for use with the ventilator, are also described. The function of the ventilator with the new valve was assessed using a piped gas supply and then reassessed when powered by the compressors.*

## Key words

*Equipment*; ventilators, portable.

Portable ventilators, to meet the demands of modern cardiopulmonary-cerebral-resuscitation (CPR) as well as for the transfer of critically ill patients within and between hospitals, are now more commonplace. The pneuPAC ventilator module has been shown to work well under adverse conditions and to be satisfactory in operation.[1] It is designed to deliver a range of tidal volumes and frequencies suitable for both adults and children.

The manufacturers have introduced an alternative patient valve which allows the choice of a fractional inspired concentration of oxygen ($F\text{IO}_2$) of 0.45 or 1.0. Two new air compressors have also been produced, one powered from mains electricity and the other by 12V DC, either from its own battery, or an external source, so that the ventilators can be used independently of compressed gas pipelines or cylinders. The performance of the pneuPAC ventilator Model 2-R, which allows the immediate selection of CPR setting, and the new patient valve were assessed, using both the air compressors and oxygen from the hospital pipeline as the gas supply.

In addition to the new patient valve and compressors there is a range of accessories that includes an airway pressure gauge, positive end expiratory pressure (PEEP) valves, high pressure relief valves and a scavenging adaptor enabling a ventilator to be constructed to meet specific needs.

## Description

### Ventilator

The pneuPAC ventilator consists of two elements, the control module and the patient valve, which are interconnected by a high pressure, small bore, nylon braided, kink proof hose. The control module is similarly linked to a high pressure oxygen supply or an air compressor that uses a Schrader type connecting probe which meets BS 5682[2] specification, and thereby allows connexion to any standard oxygen pipeline outlet in hospitals or ambulances. The gas inlet and outlet pipes are both joined to the back of the control module and cannot be wrongly connected. The ventilator specification is shown in Table 1.

### Control unit

The control module incorporates an integrated pneumatic logic control system which is powered by the gas delivered to the ventilator and is housed in a yellow case made of fire retardant polyphenylene-oxide. A single shrouded knob on the front panel controls the inspiratory and expiratory times and hence tidal volume and frequency. The technical details of the control module were

---

G.R. Park, FFARCS, Consultant in Anaesthesia and Intensive Care, A.R. Manara, MRCP, FFARCS,* A.R. Bodenham, FFARCS,† Research Registrars, C.J. Moss, MIElecIE, TEng, Medical Electronics Technician, Department of Anaesthesia, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ.

*Present address: Department of Anaesthesia, Plymouth General Hospital.

†Present address: Department of Anaesthesia, St. James Hospital, Leeds.

Correspondence should be addressed to Dr G.R. Park please.

Accepted 1 June 1988.

0003–2409/89/050419 + 06 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Technical specifications of the pneuPAC ventilator and air entrainment valve.

| | Weight (gm) | Size l × b × w or l × diameter (mm) |
|---|---|---|
| Control module | 1633 | 182 × 80 × 60 |
| Patient valve* (with air-mix control) | 190 | 100 × 123 × 70 |
| Patient valve (without air-mix control) | 83 | 88 × 97 × 67 |
| Pressure gauge (Range 0–10 kPa) | 242 | 76 × 71 × 72 |
| Pressure relief valve | 12 | 54 × 29 |
| PEEP valve | 7 | 25 × 29 |
| Frequency range | 11–21/minute | |
| Tidal volume range (ml) (No air mix) | 260–1290† | |
| Tidal volume range (with air mix) | 310–1380† | |
| I : E ratio | 1/4.5–1/1.5 | |
| Driving gas | Air, oxygen or entonox | |

* With PEEP and pressure relief valve.
† Manufacturer's specification 340–1450 ml.

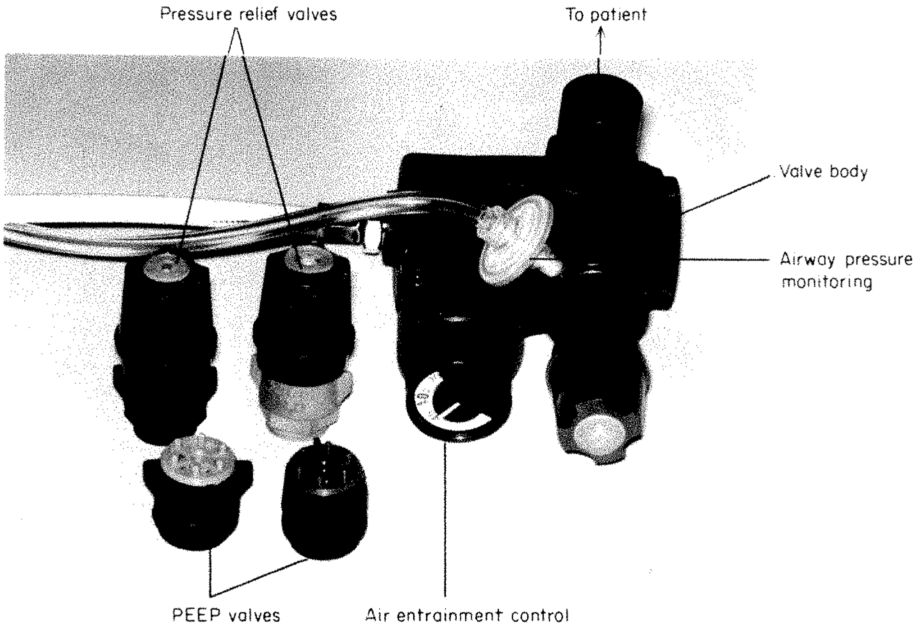


**Fig. 1.** The air entrainment patient valve.

described previously.[3] Recent modifications to the front panel include coding to indicate the appropriate settings for children and adults and the addition of a 'click-stop' mechanism, incorporated in the control knob, to allow the immediate selection of the recommended CPR settings (tidal volume 900 ml, respiratory frequency 13).[4] Essential operating instructions are clearly printed on the top of the control module.

### *Entrainment valve*

The new patient valve operates in a manner similar to that described previously for the nonentrainment valve.[3] High pressure pulses delivered by the control module move a piston against a spring to seal off the expiratory port and open the inspiratory limb to allow gas to be delivered to the patient. As the pulses terminate the spring pushes the piston back into position and allows the patient to exhale. The new valve (Fig. 1) includes a control for selection of 100% oxygen or 45% oxygen, using an air entrainment device that works on the Venturi principle. In the air-mix mode it delivers 70% filtered air/30% oxygen mixture so that the patient receives an $F\text{IO}_2$ of 0.45. The use of air entrainment allows a 65% reduction in compressed gas consumption. The inspiratory port is a standard 22/15 mm BS 3849 taper.[5] The expiratory port allows attachment of PEEP valves or a 30-mm male taper exhaust fitting for scavenging of expired gases. The pressure relief valve (4, 6 or 8 kPa) with audible alarm is screwed into a third aperture on the patient valve. The dead space of the valve is 9 ml. The valve is made from glass-filled polyphenylene-oxide and stainless steel; it can be disinfected by most methods but cannot be autoclaved [we, however, rarely sterilise patient valves of transport ventilators and prefer to rely on heat and moisture exchanging bacterial filters (HMEF)].[6]

The airway pressure gauge clips onto the control module. It is connected to the patient valve by small bore transparent tubing that is clipped to the control module output hose and attached to a connector seated below the pressure relief valve. It is impossible to attach any of the fittings to the valve wrongly. The new entrainment valve and accessories can be fitted to any of the earlier control modules.

### *Compressor*

The air compressor is of rugged construction and delivers filtered, cooled, compressed air to a Schrader outlet (Fig. 2). Four models are available, two powered by mains electricity (110 or 220/240V ac), and the others by 12 or 24V dc. We examined only the 220/240V ac and the 12V dc models. All models are oil-free diaphragm compressors. The gas supplied by the compressor is cooled by a refrigerant drier (using the Peltier effect) to extract moisture from the compressed air before delivery to the ventilator; this thereby protects the latter from corrosion

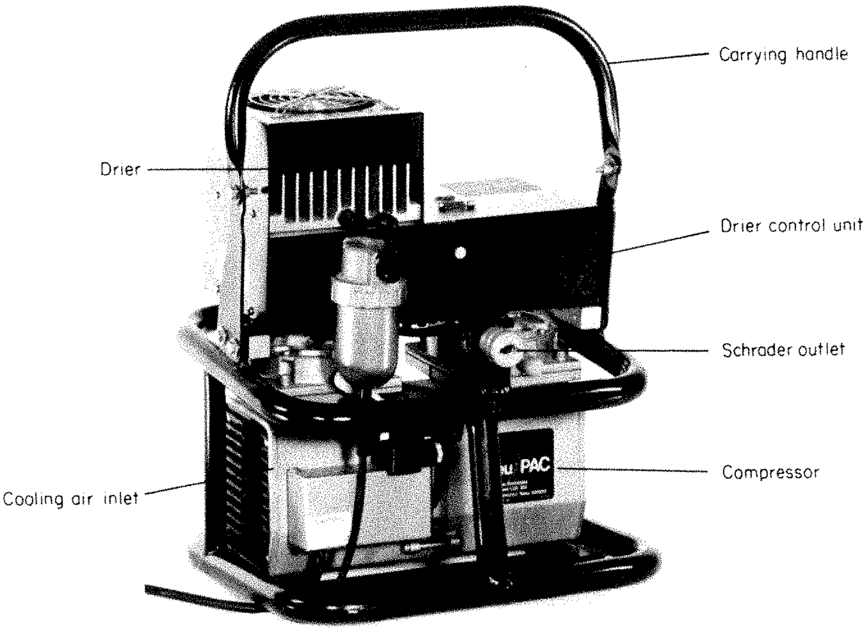


**Fig. 2.** The mains powered air compressor.

and microbiological colonisation. The commercially available Schrader outlet will accept both air and oxygen probes and this contravenes the usual practice of not allowing devices using oxygen to connect to a compressed air source. The manufacturers have agreed to label prominently the compressor with a warning that it is a supply of 'air only', to decrease the risk of unintentional, hazardous use of air when oxygen may be necessary. A recent addition to the compressor is an inlet device that enables 3 litres/minute of oxygen to be added to the air, to increase the $F_{IO_2}$ of the gas used to supply the ventilator. The effects of this on $F_{IO_2}$ are reported later.

## Assessment of accuracy of ventilator and associated equipment

### *Method*

The ventilator was used to ventilate a lung ventilator performance analyser (Medishield lung ventilator performance analyser, British Oxygen Company)[7] at varying compliance and resistance settings, as suggested in BS 6850, 1987.[8] The ventilator was then assessed in a manner similar to that described previously[9] using a pressure relief valve set to 5.88 kPa. This pressure was exceeded at tidal volume settings greater than 900 ml; volumes in excess of this were not studied. Studies of derived gas flows were measured using a pneumotachograph head connected to a Furness micromanometer and Mercury integrator.

Inspired oxygen and inspiratory pressure were measured on the inspiratory limb using a calibrated polarographic analyser (Instruments Laboratories Ltd) and a pressure transducer (Pye Ether) respectively. Expired volumes were measured for each setting over a period of 100 cycles using a dry gas meter (Parkinson Cowan, Thorn EMI). The tidal volume was then calculated by dividing the total volume by 100.

The accuracy of the airway pressure gauge was assessed using a 1.1-m column of water connected through low compliance tubing. Pressure within the system was adjusted using a syringe, and the accuracy of the gauge compared to the water column at 10-cm intervals. Both PEEP valves and pressure limiting valves were tested using air flows of 10, 20 and 30 litres/minute through them; pressure was similarly measured through a side arm using a water column.

## Results

The results obtained, when the ventilator was driven using pipeline oxygen and the air compressor with and without pipeline oxygen, are summarised in Tables 2, 3 and 4. The oxygen concentration in the air-mix mode only varied from 45% to 47% over the selected range of ventilator and test lung settings, when pipeline oxygen is used to drive the system. The delivered oxygen varied from 49% to 67%, from largest to smallest tidal volumes tested, when the air compressor had its added 3-litre oxygen supply. The use of the compressor, added oxygen and the air-mix gave delivered oxygen concentrations in the range 41–45%. The frequency setting was sufficiently accurate over all ranges, but reproducible, exact positioning of the control knob of the ventilator is not possible at all settings due to the lack of 'click stops'. All measured tidal volumes were less than the ventilator settings and are given as percentage less than the setting. The error of the tidal volume control mean (range) was 4.1% (2–5%) with no air-mix and 16.75% (14–19%) with air-mix when the ventilator was powered by piped oxygen. The error was 8.1% (6.2–10%) with no air-mix and 21.5% (21–22%) with air-mix mode, when the compressor was used without its added oxygen supply. These errors were 6% (5–7%) and 19% (18–20%) respectively when the compressor used its added oxygen supply. The manufacturers recommend that the compressor should only be used with the valve in the air-mix position. Our findings, of a greater inaccuracy in this position with

**Table 2.** Accuracy of the pneuPAC ventilator, when driven by high pressure (410 kPa) oxygen from pipeline supply, using the test lung at different compliance and resistance settings.

| Ventilator settings | | | Test lung settings | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | C 0.5 R 0.5 | | | C 0.2 R 0.5 | | | C 0.1 R 0.5 | | | C 0.5 R 2 | | |
| *V*T | f | | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ |
| 340 | 21 | Air-mix | 297 | 20.0 | 0.45 | 296 | 19.8 | 0.46 | 292 | 19.6 | 0.47 | 294 | 20.0 | 0.47 |
| | | No air-mix | 363 | 19.3 | 1.0 | 363 | 19.4 | 1.0 | 356 | 19.3 | 1.0 | 360 | 19.3 | 1.0 |
| 400 | 19 | Air-mix | 350 | 17.7 | 0.45 | 348 | 17.6 | 0.45 | 340 | 17.9 | 0.46 | 344 | 17.3 | 0.47 |
| | | No air-mix | 424 | 17.6 | 1.0 | 428 | 17.4 | 1.0 | 424 | 17.6 | 1.0 | 424 | 17.4 | 1.0 |
| 500 | 16 | Air-mix | 432 | 15.5 | 0.45 | 420 | 15.5 | 0.45 | 406 | 15.6 | 0.45 | 410 | 15.4 | 0.46 |
| | | No air-mix | 533 | 15.4 | 1.0 | 516 | 15.6 | 1.0 | 516 | 15.5 | 1.0 | 524 | 15.3 | 1.0 |
| 700 | 14 | Air-mix | 588 | 13.1 | 0.45 | 572 | 13.0 | 0.45 | 555 | 13.1 | 0.46 | 550 | 13.3 | 0.47 |
| | | No air-mix | 746 | 13.0 | 1.0 | 736 | 12.8 | 1.0 | 732 | 13.0 | 1.0 | 708 | 13.3 | 1.0 |
| 900 | 13 | Air-mix | 772 | 12.5 | 0.45 | 656 | 12.3 | 0.46 | | | 0.46 | 648 | 12.5 | 0.47 |
| | | No air-mix | 866 | 12.3 | 1.0 | 860 | 12.2 | 1.0 | | | 1.0 | 842 | 12.5 | 1.0 |
| Mean percentage error in delivered tidal volume | | Air-mix | −14% | | | −17% | | | −17% | | | −19% | | |
| | | No air-mix | −5% | | | −5% | | | −4.4% | | | −2% | | |

*V*T, tidal volume (ml); *F*IO$_2$, fractional inspired oxygen concentration; f, frequency (breaths/minute); C, compliance; R, resistance (kPa/litres/second).

**Table 3.** Accuracy of the pneuPAC ventilator, when driven by the air compressor without its added oxygen supply, using the test lung at different compliance and resistance settings.

| Ventilator settings | | | Test lung settings | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | C 0.5 R 0.5 | | | C 0.2 R 0.5 | | | C 0.1 R 0.5 | | | C 0.5 R 2 | | |
| *V*T | f | | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ |
| 340 | 21 | Air-mix | 279 | 22.2 | 0.21 | 286 | 21.4 | 0.21 | 284 | 20.7 | 0.21 | 292 | 21.1 | 0.21 |
| | | No air-mix | 298 | 22.2 | 0.21 | 328 | 21.8 | 0.21 | 336 | 20.7 | 0.21 | 330 | 20.8 | 0.21 |
| 400 | 19 | Air-mix | 342 | 19.1 | 0.21 | 324 | 19.1 | 0.21 | 344 | 17.4 | 0.21 | 330 | 18.9 | 0.21 |
| | | No air-mix | 388 | 19.1 | 0.21 | 382 | 19.1 | 0.21 | 404 | 17.6 | 0.21 | 398 | 18.8 | 0.21 |
| 500 | 16 | Air-mix | 398 | 17.1 | 0.21 | 396 | 16.6 | 0.21 | 408 | 15.9 | 0.21 | 398 | 16.5 | 0.21 |
| | | No air-mix | 470 | 16.7 | 0.21 | 474 | 16.7 | 0.21 | 496 | 15.7 | 0.21 | 484 | 16.4 | 0.21 |
| 700 | 14 | Air-mix | 534 | 14.4 | 0.21 | 572 | 14.3 | 0.21 | 510 | 14.3 | 0.21 | 522 | 14.0 | 0.21 |
| | | No air-mix | 640 | 13.9 | 0.21 | 636 | 13.9 | 0.21 | 628 | 13.8 | 0.21 | 636 | 13.6 | 0.21 |
| 900 | 13 | Air-mix | 644 | 13.1 | 0.21 | 620 | 13.0 | 0.21 | 580 | 13.3 | 0.21 | 614 | 13.3 | 0.21 |
| | | No air-mix | 728 | 12.8 | 0.21 | 722 | 12.8 | 0.21 | 716 | 12.6 | 0.21 | 720 | 12.6 | 0.21 |
| Mean percentage error in delivered tidal volume | | Air-mix | −21% | | | −21% | | | −22% | | | −22% | | |
| | | No air-mix | −10% | | | −9.1% | | | −6.2% | | | −7% | | |

**Table 4.** Accuracy of the pneuPAC ventilator, when driven by the air compressor with its added oxygen supply, using the test lung at different compliance and resistance settings.

| Ventilator settings | | | Test lung settings | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | C 0.5 R 0.5 | | | C 0.2 R 0.5 | | | C 0.1 R 0.5 | | | C 0.5 R 2 | | |
| *V*T | f | | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ | *V*T | f | *F*IO$_2$ |
| 340 | 21 | Air-mix | 294 | 22.6 | 0.41 | 301 | 20.0 | 0.43 | 300 | 19.7 | 0.44 | 292 | 20.3 | 0.45 |
| | | No air-mix | 326 | 21.7 | 0.64 | 348 | 20.7 | 0.65 | 340 | 20.0 | 0.65 | 340 | 20.0 | 0.67 |
| 400 | 19 | Air-mix | 346 | 18.2 | 0.41 | 356 | 17.6 | 0.43 | 348 | 17.1 | 0.44 | 340 | 17.5 | 0.45 |
| | | No air-mix | 390 | 18.6 | 0.62 | 406 | 18.2 | 0.63 | 404 | 17.1 | 0.63 | 394 | 16.9 | 0.64 |
| 500 | 16 | Air-mix | 412 | 16.2 | 0.41 | 416 | 15.4 | 0.43 | 405 | 16.1 | 0.44 | 418 | 15.6 | 0.45 |
| | | No air-mix | 474 | 16.4 | 0.60 | 490 | 15.6 | 0.60 | 470 | 16.2 | 0.61 | 496 | 15.6 | 0.62 |
| 700 | 14 | Air-mix | 558 | 13.6 | 0.41 | 548 | 13.3 | 0.43 | 530 | 13.4 | 0.43 | 544 | 13.5 | 0.45 |
| | | No air-mix | 648 | 13.6 | 0.55 | 640 | 13.3 | 0.54 | 640 | 13.3 | 0.54 | 646 | 13.2 | 0.56 |
| 900 | 13 | Air-mix | 654 | 12.2 | 0.41 | 644 | 12.5 | 0.42 | 600 | 12.7 | 0.42 | 636 | 13.5 | 0.45 |
| | | No air-mix | 744 | 12.5 | 0.50 | 744 | 12.4 | 0.49 | 720 | 12.4 | 0.49 | 734 | 12.3 | 0.50 |
| Mean percentage error in delivered tidal volume | | Air-mix | −19% | | | −18% | | | −20% | | | −19% | | |
| | | No air-mix | −7% | | | −5% | | | −7% | | | −6% | | |

no advantages, do not support this recommendation. A warning to this effect needs to be placed on the compressor.

Measurement of the ventilator's oxygen consumption showed that a standard E-size cylinder (680 litres) would last for 65 minutes, with the ventilator set to deliver its maximum minute volume not using air mix.

Analysis of the pressure, flow and volume waveforms confirmed that the ventilator functions as a constant flow generator with time cycling, irrespective of whether the air-mix facility is used or not (Fig. 3).

The airway pressure gauge varied by ±0.2 kPa throughout its range. Similarly the PEEP valves were accurate to 0.1 kPa. The pressure relief valves differed from their specified pressures by −0.6 kPa (8.0 kPa valve) and −0.2 kPa (4.0 kPa valve). These differences are unlikely to be significant in clinical practice.

Resuscitation ventilators must continue to function if the patient valve becomes filled with vomit. To simulate the effects of vomit, two parts of beef and vegetable baby food (Heinz Ltd) was mixed with one part tap water and warmed to 37°C. An anaesthetic facemask was fitted to the

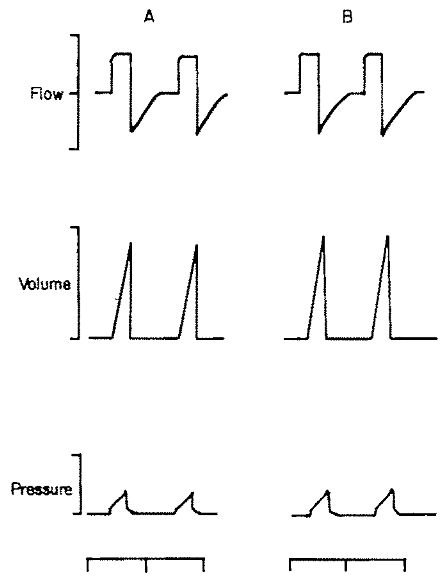


**Fig. 3.** Flow, volume and pressure waveforms with the patient valve in the air mix (A) and no air mix (B) modes.

**Table 5.** Technical specification of the compressors.

| | Mains powered | Battery powered |
|---|---|---|
| Power source | 220/240 V 50 Hz ac<br>110 V 60 Hz ac | 12 V lead acid battery |
| Power consumption | 75 watts | |
| Weight | 9.2 kg | 8.4 kg |
| + drier | 13.2 kg | 12.4 kg |
| Operating temperature range | 0–40°C | |
| Dimensions | 350 × 330 × 360 mm | 260 × 335 × 350 mm |
| Rating | 2000 hours continuous use | |
| Duration | | 2.5 hours continuous use |

patient valve. The patient valve and mask were inverted and, with the ventilator functioning, approximately 175 ml of the simulated vomit was poured into the mask.[7] The procedure was repeated at every tidal volume setting using both the air entrainment and no air entrainment modes. The valve continued to function at all settings and cleared the 'vomit' within 2–3 cycles.

### *Compressor*

The outlet pressure was measured continuously in both compressors throughout the test period by a Bourdon gauge inserted into a side arm of the high pressure gas outlet. The pressure remained constant at all times at 410 kPa which is within the operating range of the ventilator. The technical specifications of the compressors are shown in Table 5.

### *Mains powered*

The unit is powered by 220/240 V ac, but since it was originally designed only for use outside hospitals, its electrical construction did not meet the requirements of BS 5724.[10] The live and neutral wires were not fused; there was no double pole mains switch, the mains flexible cable did not terminate into a labelled connector block, nor did the internal power supply comply with Class 2 requirements. The basic requirements of this standard include having only two core mains cable (i.e. no earth conductor) and that supplemental insulation should be provided over and above that found in normal practice. If these requirements are met, then before a piece of equipment can become a hazard, two safety mechanisms have to fail simultaneously. The original compressor therefore was not suitable for use in hospitals, but the manufacturers have modified it to comply with the requirements.

### *Battery powered*

The unit is powered by an internal lead acid rechargeable battery, with the electrolyte solution in jelly form, which allows the ventilator to run for 2 continuous hours. A connecting lead is supplied which allows it to be powered by an external 12 V source such as a car battery.

The battery-powered compressor functions and behaves in a similar way to the mains-driven compressor. The theoretical possibility of spillage from the lead acid battery prevents the compressor's use with this power source on aircraft, but this should not limit it in the clinical situation.

### *Practical experience with the ventilator*

The ventilator was used in the Intensive Care Unit of this hospital. It performs satisfactorily although the pressure relief valve, PEEP valve, air entrainment control and airway pressure monitoring system all make the valve rather bulky. This may cause difficulties when a patient's lungs are artificially ventilated through a mask. The large minute volumes make it difficult to avoid hyperventilation of small children especially when a tracheal tube is in place.

The mains compressor is bulky and noisy but appears suitable to power the ventilator when a compressed gas supply is otherwise unavailable or in short supply. The addition of supplemental oxygen allows it to be used when a higher $F\text{IO}_2$ is required.

## Discussion

The requirements of a resuscitation ventilator and those for one used to transport critically ill patients[11,12] have been described, and while many of the demands are common to both there are substantial differences (Table 6).

Resuscitation ventilators tend to be used by staff with limited training and the operation of their controls must therefore be simple and self evident. The ventilator may be exposed frequently to adverse environmental conditions including rain, dirt and dust, and accidental dropping. It must therefore be robust and the working parts protected from the environment. Air entrainment is undesirable since patients may require rescue from a toxic environment when this would be dangerous.[13] An $F\text{IO}_2$ of 1.0 will ensure adequate oxygenation and, since most attempts are of short duration, the problems of pulmonary oxygen toxicity do not arise.

Ventilators used for transport within and between hospitals tend to be handled by highly trained personnel who are able to deal with more complex equipment. Transport ventilators are usually employed in a less hostile environment than resuscitation ventilators, although they may still be dropped and must remain robust. Patient needs are more demanding, and the transport ventilator must be an effective substitute for their bedside ventilator, with the ability to apply PEEP and monitor airway pressure. Transfers must, wherever possible, take place in a

**Table 6.** The similarities and differences in requirements of transport and resuscitation ventilators.

| Differences | | Similarities |
|---|---|---|
| *Transport* | *Resuscitation* | Robust, lightweight and compact |
| Adjustable PEEP | Not essential | Safe and foolproof to use |
| Variable $F\text{IO}_2$ | Fixed $F\text{IO}_2$ | Clear instructions printed on the ventilator |
| | No air entrainment in toxic atmosphere | Controls easily identifiable in the dark |
| | | Requires minimal servicing |
| Airway pressure gauge | Not essential | Time/volume cycled |
| Compatible with HMEF | Not essential | Adult or paediatric use |
| Can be used as a resuscitation ventilator | | Audible pressure relief valve |
| | | Compatible with facemasks and tracheal tubes |
| | | Autoclavable parts and failsafe reassembly |
| | | Reliable in wet and dirty conditions |
| | | Alternative power source should gas supply be unavailable or fail |
| | | Inexpensive |

calm, unhurried manner to expose the patient to minimum risk; this will necessarily prolong the period of transfer, so heat and moisture loss must be prevented and compatibility with heat and moisture exchangers, which are effective in achieving this aim, is essential. Unnecessary ventilation with 100% oxygen for prolonged periods is both hazardous for the patient[14] and expensive of compressed gas; since patients are not transferred through toxic atmospheres, air entrainment can be utilised to overcome these problems. Air entrainment can be achieved either in the control unit, a method used in ventilators such as the Drager Oxylog[8] or at the patient valve as in the pneuPAC. The latter method offers greater flexibility with the option of interchangeable valves, whilst the former results in a smaller patient valve but with increased size and weight of the control unit.

Great attention has been paid to the design of bedside intensive care unit ventilators while until recently scant consideration was given to ventilators for transporting critically ill patients; many units relied on resuscitation ventilators for this. The ideal is to have purpose designed ventilators, but systems such as the pneuPAC, that utilise the similarities between the two types of ventilators with 'add-on' parts, allow flexibility and enable a cost-effective ventilator to be built to suit the specific needs and training of the users.

In conclusion, new additions to the pneuPAC range of portable lung ventilators are described. They offer, when added to the basic control module, a cost-effective, comprehensive, flexible and robust ventilator system that can be tailored to suit the requirements of a ventilator used during the resuscitation and transport of critically ill patients.

## References

1. Harber T, Lucas BGB. An evaluation of some mechanical resuscitators for use in the ambulance service. *Annals of the Royal College of Surgeons* 1980; **62:** 291–3.
2. British Standard Specification for terminal units, hose assemblies and their connectors for use with medical gas pipeline systems BS 5682, British Standards Institution 1984.
3. Adams AP, Henville JD. A new generation of anaesthetic ventilators. The pneuPAC and Penlon A-P. *Anaesthesia* 1977; **32:** 34–40.
4. Standards and guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC). *Journal of the American Medical Association* 1986; **255:** 2905–84.
5. British Standards for breathing attachments for anaesthetic apparatus BS 3849 British Standards Institution 1965.
6. Shelly MP, Park GR, Warren RE, Whetstone RJ. Portable lung ventilators: the potential risk from bacterial colonisation. *Intensive Care Medicine*, 1986; **12:** 328–31.
7. Chakrabrati MK, Sykes MK. Evaluation of the lung ventilator performance analyser. *Anaesthesia* 1976; **31:** 521–8.
8. British Standard specification for ventilatory resuscitators BS 6850, British Standards Institution 1987.
9. Park GR, Johnson S. A ventilator for use during mobile intensive care and total intravenous anaesthesia. The Drager Oxylog. *Anaesthesia* 1982: **37:** 1204–8.
10. British Standard for medical electrical equipment; Part 1. BS 5724. British Standards Institution 1979.
11. Gray AJG. Portable lung ventilators. *British Journal of Hospital Medicine* 1981; **25:** 173–8.
12. Marsh RHK, Mc Ledingham I. Equipment for mobile intensive care. *British Journal of Hospital Medicine* 1981; **25:** 377–85.
13. Harries MG. Portable ventilators under field conditions. *Anaesthesia* 1983; **38:** 279–81.
14. Frank L, Massaro D. The lung and oxygen toxicity. *Archives of Internal Medicine* 1979; **139:** 347–50.

*Anaesthesia*, 1989, Volume 44, pages 425–427

APPARATUS

# A modified expiratory valve for teaching

A. J. SANSOME AND R. BACON

## Summary

*The shrouding of anaesthetic expiratory valves prevents the anaesthetist from either seeing valve disc movement or hearing clearly the escape of gas during expiration. A modification to one type of valve (Medishield II) is described which replaces this lost information by providing a direct indication of valve opening.*

## Key words

*Equipment*; valves.

The widespread use of shrouded expiratory valves in anaesthesia to reduce contamination of the operating theatre atmosphere prevents the anaesthetist from either seeing the valve disc lift or hearing the hiss of escaping gas during expiration. The experienced anaesthetist can easily compensate for loss of this information, while the trainee is less able to do so. It was therefore our intention to produce a simple modification which would restore this lost information, without adversely affecting the opening pressure or resistance to flow of the expiratory valve.

## Description

The Medishield II shrouded expiratory valve (Ohmeda Ltd) is widely available and was chosen as the basis of this modification. A plastic shroud surrounds the valve to facilitate the scavenging of expired gas. The valve proper consists of a circular knife edge seat on which rests a light plastic disc located by a central rod running in a tubular guide. A light spring is located between the top of the valve body and the disc; as a result the opening pressure can be increased by screwing down the top of the valve casing to compress the spring.

The modification consists of remaking both the valve seat and the disc. The replacement valve seat is constructed so that the knife edged contact area is recessed 3.5 mm into a short tube or chimney with a diameter 0.05 mm greater than that of the valve disc (Fig. 1). The valve disc is unchanged but is remanufactured to increase the length of its guide to 4 cm, while the top 3 mm are painted red. The adjustable top of the valve body contains a sleeve which locates the valve guide and this is drilled out to a diameter of 2.5 mm to extend the sleeve through the top of the valve body (Fig. 2).

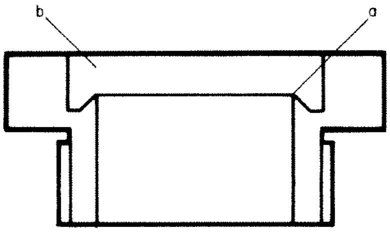


**Fig. 1.** Cross section through the modified valve seat, (a) knife edged seat, (b) tubular chimney.

## Assessment of performance

The opening pressure and the pressure drop across both modified and standard valves were measured with a water manometer, as the flow of room air was increased to 1.25 litres/second. This was then repeated with air saturated with water vapour at 37°C. Measurements with both the modified valve and its standard precursor were repeated three times and the means calculated (Table 1).

The opening pressure of the modification was slightly lower than that of the original when measured with dry gas (0.11 kPa/0.14 kPa), but slightly higher when air saturated with water vapour was used (0.19 kPa/0.14 kPa). The modification was also subject to a small amount of hysteresis when wet; the opening pressure was 0.19 kPa while the pressure drop at 0.15 litres/second was 0.11 kPa.

Once open, as flow was increased to 1.25 litres/second the pressure drop across the modified valve remained slightly below that of the standard, to reach 0.29 kPa

---

A. J. Sansome, FFARCS, Senior Registrar, Shackleton Department of Anaesthetics, R. Bacon, BSc, PhD, Senior Medical Engineer, Department of Medical Engineering, Southampton General Hospital, Tremona Road, Southampton, Hants.

Accepted 18 October 1988.

0003–2409/89/050425 + 03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Mean pressure drops across both standard and modified valves as the flow of both dry air and air saturated with water vapour at 37°C were increased to 1.25 litres/second.

| Flow litres/second | Pressure drop across valve (kPa) | | | |
|---|---|---|---|---|
| | Standard | | Modified | |
| | Dry | Wet | Dry | Wet |
| Opening pressure | 0.14 | 0.14 | 0.11 | 0.19 |
| 0.05 | 0.14 | 0.135 | 0.11 | 0.11 |
| 0.067 | 0.14 | 0.14 | 0.11 | 0.11 |
| 0.1 | 0.15 | 0.14 | 0.115 | 0.12 |
| 0.13 | 0.15 | 0.15 | 0.13 | 0.13 |
| 0.167 | 0.155 | 0.15 | 0.13 | 0.14 |
| 0.25 | 0.16 | 0.14 | 0.145 | 0.14 |
| 0.33 | 0.17 | 0.17 | 0.16 | 0.16 |
| 0.42 | 0.19 | 0.18 | 0.17 | 0.17 |
| 0.5 | 0.195 | 0.19 | 0.18 | 0.18 |
| 0.58 | 0.205 | 0.2 | 0.19 | 0.18 |
| 0.67 | 0.21 | 0.21 | 0.2 | 0.2 |
| 0.83 | 0.23 | 0.235 | 0.22 | 0.22 |
| 1.0 | 0.27 | 0.27 | 0.245 | 0.25 |
| 1.17 | 0.29 | 0.30 | 0.28 | 0.28 |
| 1.25 | 0.31 | 0.31 | 0.29 | 0.29 |

compared with 0.31 kPa at 1.25 litres/second, both wet and dry (Fig. 3). Comparison of the pressure drop across the dry or wet standard and modified valves using a paired *t*-test showed that the pressure drop across the modified valve was less than that across the standard valve ($p < 0.001$ for dry and $p < 0.05$ for wet valves).

## Discussion

The modified valve was 70 mg lighter than the original at 800 mg and this explains our findings of both a lower opening pressure and a lower pressure drop throughout the range of flows over which the valves were compared. This difference is partially offset at higher flow rates because the lifting of the disc forced by the added sleeve around the valve seat starts to compress the spring, to restrict valve opening. The hysteresis on opening when wet, due to the surface tension of water lining the sleeve above the valve seat, was only 0.08 kPa, 0.05 kPa greater than the standard valve. This modification has been used as part of a Mapleson A breathing system to teach a number of novice anaesthetic senior house officers.[1]

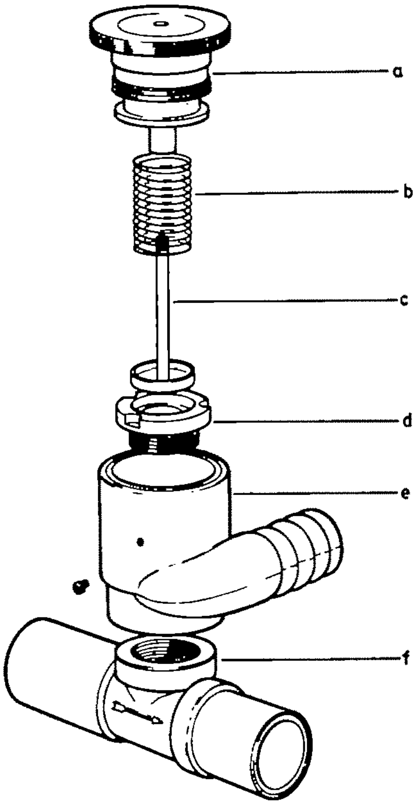


**Fig. 2.** Expanded view of the whole valve showing the relationship between its component parts. (a) adjustable top, (b) spring, (c) modified valve disc, (d) modified valve seat, (e) shroud and (f) body.

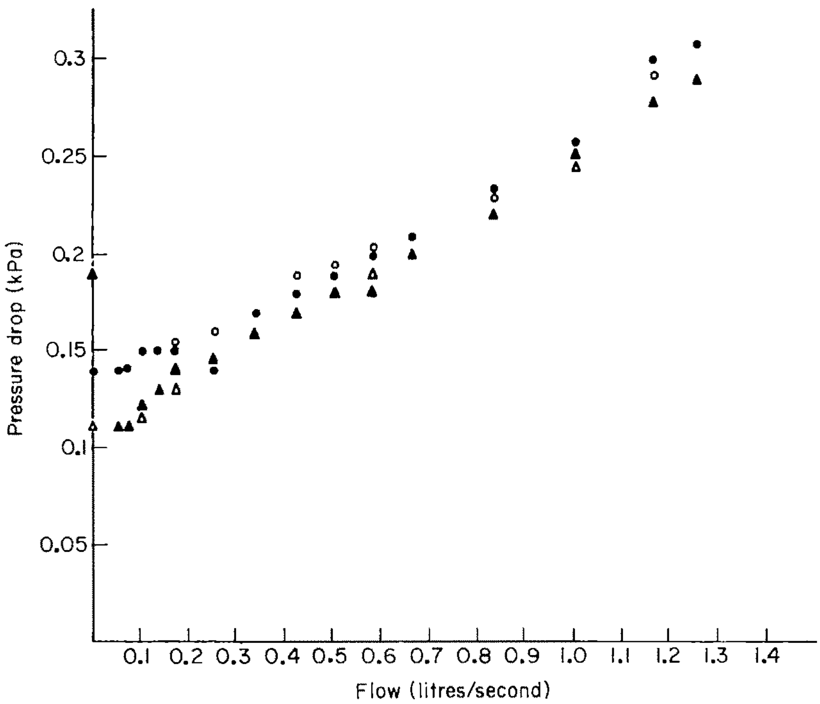


**Fig. 3.** Pressure drop across the standard valve, dry ○ and wet ●, and the modification, dry △ and wet ▲.

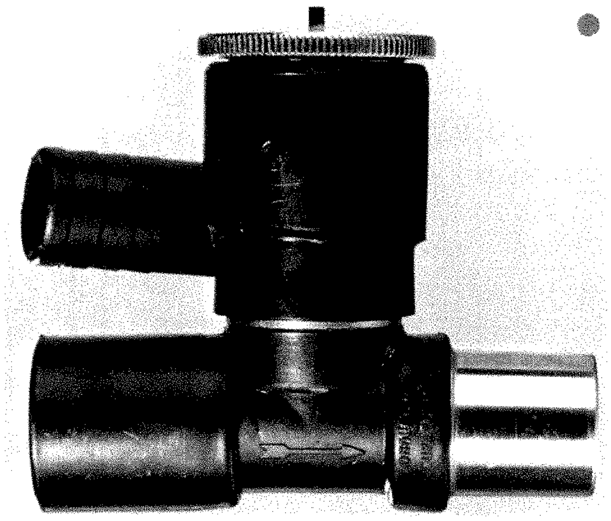


**Fig. 4.** The modified Medishield type II expiratory valve.

The state of the valve is continuously apparent and may help in the diagnosis of airway obstruction when the indicator remains in the up (valve open) position. A large leak from the breathing system is noticed when the indicator remains in the down (valve closed) position, while spontaneous ventilation in the absence of a significant leak results in the indicator bobbing up and down with breathing.

The Medishield II is widely available and the modification sufficiently straightforward to be within the capabilities of most departments of medical engineering.

## Reference

1. MAPELSON WW. The elimination of rebreathing in various semi-closed anaesthetic systems. *British Journal of Anaesthesia* 1954; **26:** 323–32.

*Anaesthesia*, 1989, Volume 44, pages 428–431

SPECIAL ARTICLE

# Intensive care in the United Kingdom: report from the King's Fund panel *

**Key words**

*Intensive care.*
*Anaesthesia*; audit.

Intensive care units (ICU) epitomise the challenge of high technology medicine. They make heavy demands in terms of staff, equipment and other resources yet they have the potential to save lives and increase the chances of survival where alternative therapies have nothing to offer. Furthermore, while they undoubtedly bring benefit to some patients, ICUs also result in loss of the patient's dignity, privacy and autonomy. Balancing benefits and costs is not easy, and it was this issue that a multidisciplinary panel convened by the King's Fund sought to address at a number of meetings in 1988. The panel reviewed the published literature on ICUs (see Bibliography), considered submissions from a small number of invited experts, and drew on the experience of its members. It soon became apparent that lack of data in the United Kingdom would make it impossible to prepare a definitive statement on the role of ICUs in the National Health Service (NHS). Accordingly, the panel decided to produce a report summarising the current state of knowledge about intensive care, highlighting the absence of evidence and calling for a substantial programme of research.

## Definition of intensive care

A definition favoured by the panel is: *A service for patients with potentially recoverable diseases who can benefit from more detailed observation and treatment than is generally available in the standard wards and departments.*

An ICU is then a *place* and not a form of treatment. It provides special skills and experience from medical and nursing staff for the care of critically ill patients and particularly those in whom there is expectation of failure of one or more organ systems. It also provides a centre for physiological measurements, nursing procedures and therapeutic manoeuvres which are not practicable in the general wards. Procedures undertaken in an ICU are done there on the assumption, understandable but unproven, that the concentration of special facilities and expertise gives better results and reduces costs.

What intensive care provides varies according to the activities of the relevant hospital and the predominant mix of patients admitted for intensive attention. The outcome of intensive care depends not only on the facilities provided in the unit and the skill and timing with which they are administered, but also on the case mix of problems presented by the surgeons and physicians who make the initial decisions which result in their patients requiring intensive care. Generalisation about intensive care units may be quite inappropriate unless their heterogeneity is better recognised. Hospitals which specialise in a particular condition may regard as routine a procedure considered specialised elsewhere, and so undertake it in a ward or department other than ICU. There are relatively few conditions for which an ICU is essential, and few procedures which can only be done, or done safely, in such a unit.

Much of intensive care involves temporary replacement of the function of one or more organs, for example ventilation for respiratory failure or dialysis for renal failure, and it is in these cases of single organ failure that the best results are achieved. It is also used for monitoring to detect and respond rapidly to serious complications in patients judged to be at risk of becoming critically ill. The bulk of intensive care work in the UK today concerns the management of patients who, after trauma, major surgery or overwhelming illness, suffer from malfunction of several organs. The outcome for such patients is much more unpredictable, and depends fundamentally on the severity of the presenting problems.

## Criteria for admission to ICU

Intensive care should be given primarily in the expectation of beneficial consequences when such benefits can be achieved at acceptable cost. It should not be provided in situations where possible harm outweighs the remote prospects of benefit. Within a group of patients for whom intensive care is considered, the likely outcome of such care is a major consideration. The panel suggests that a simple scale is used: expected to survive; potentially recoverable (a good chance); prognosis uncertain; death probable shortly whatever is done; and death apparently imminent. *In view of public expectations of what medicine can achieve the panel recommend that in the UK intensive care should be provided for the first two of these categories.*

It may also be appropriate to admit potential organ donors (that is, those patients who fulfil the criteria o brain stem death, or are expected to do so) because procedures such as mechanical ventilation are required to

---

* See appendix.

Correspondence to Dr J. Spiby, King's Fund Centre for Health Services Development, 126 Albert Street, London NW1 7NF.

Accepted 14 February 1988.

0003–2409/89/050428 + 04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

keep the organs in good condition. *In such cases the recommended policy is to provide optimal care for the dying patient until it is agreed that further therapy is useless, when there is a shift in emphasis from prolongation of life to the maintenance of organ viability.*

There is a more difficult problem with those whose prognosis is uncertain because these patients will eventually be reclassifiable into one of the other categories. In the absence of sound data on which to base decisions these patients should also be treated in ICUs. *It is this group for whom there is an urgent need to conduct clinical trials to evaluate the need for intensive care.*

Patients whose death is probable shortly whatever is done provide a different dilemma. It is often possible to produce temporary improvement and to allow time for relatives and the medical team to come to terms with the inevitability of death. It is in these cases that the question of benefit to the patient is most difficult to assess and here also that the question of the use of resources which might benefit others instead must be considered.

*The panel recommends that each ICU should prepare a set of guidelines setting out criteria for admission to the unit to help doctors and other staff determine priorities for treatment.*

### *The concept of benefit*

There is often disagreement about what constitutes benefit. Doctors and others disagree about the probability of the benefit and about degree of benefit that should be regarded as worthwhile. In such cases, benefit should be assessed not only in terms of survival but also in terms of the quality of life.

The concept of benefit has been the subject of numerous interpretations. The panel considered the question of whose judgement of benefit should prevail in doubtful cases. The Hippocratic (also the British and the American Medical Associations') view is that the physician should benefit the patient according to his/her ability and judgement.

This statement is paternalistc and depends solely on the doctors' subjective judgement. It makes no provision for the autonomy of the patient and as an extreme has even been evoked in defence of bizarre experimental therapy and of enforced feeding and unwanted invasive treatment. The panel prefers the following: the physician should benefit the patient according to the most objective judgements available unless the patient expresses a competent and informed wish for an alternative course.

Our firm support of the right to make an informed decision to forego intensive care or any other therapy should not be construed as an endorsement of euthanasia or assisted suicide, active or passive. Moreover, the right to refuse intensive care should be exercised only by an informed person who is evidently rational and competent. In cases in which competence cannot be assessed, decisions must rest with the doctor, but always in the context of close consultation with the family, and a presumption in favour of the preservation of life must predominate. Conversely, there is no moral or legal obligation to provide treatment on request when there would appear to be no possibility of benefit.

An ability to provide a more accurate prognosis than is possible at present would help avoid some of the conflicts which arise. Severity of disease scores such as the Apache II (acute physiology and chronic health evaluation) score have a good deal to recommend them, provided they are not applied rigidly in individual cases. Selection for intensive care should be based on broad concepts of prognosis derived from statistical analysis of comparable cohorts of patients backed up by sound clinical trials. Such data are sadly deficient in the field of intensive care in the UK.

### Criteria for discharge from ITU

Four broad situations can be envisaged: the patient has recovered and is stable; the immediate threat has been alleviated but the patient remains at risk unless under close observation; the immediate threat has been alleviated but the patient is expected to die shortly; and death is agreed to be imminent, even if intensive care is continued.

Patients in the first category should be discharged as soon as possible. Those in the second may be discharged or retained depending on the needs of other patients and the available facilities elsewhere in the hospital.

Patients who are stable but expected to die can be discharged from the ICU but the panel recognises that in some circumstances this may generate a sense of rejection in patients and family at a time of particular distress. In other situations, the atmosphere of another department may be a better environment in which to come to terms with the patient's position. Competing pressures in ICU or the general ward will inevitably affect this decision.

Withdrawal of support for patients in whom the outcome looks hopeless is always difficult. Often one manifestation of the disease can be alleviated when the underlying illness cannot be reversed. This ability to achieve limited success, and the rapidity with which deterioration and death follows cessation of treatment, make it difficult to withdraw support. The decision is then how best to terminate unsuccessful management.

Sometimes it is necessary to delay the implementation of decisions to withdraw treatment while relatives assimilate and come to terms with the situation. Part of the cost of intensive care is incurred by responding to these humanitarian requirements as distinct from those relating simply to the patient's prognosis. Competing pressures may restrict the ability of an ICU to devote more than a limited resource to caring for the terminally ill, a task which may sometimes be better undertaken elsewhere. Relatives should be kept informed, at all stages during treatment, of the patient's condition and prognosis, and any information about withdrawal of support must always coincide with discussion of what will be done to ensure comfort and dignity.

### Criteria for the use of various interventions

The reasons for intervention in intensive care include diagnosis, monitoring and treatment. Invasive interventions give rise to most concern because they can result in unjustified discomfort, harm and unnecessary expense if used routinely rather than when specifically indicated. Careful audit is needed, particularly when procedures initiated for diagnostic purposes are continued as a means of monitoring. This progression is only justified if there is a significant risk of change and earlier or more accurate recognition of it would influence outcome. Again, the panel recommends that each ICU should prepare a set of *written guidelines* on the use of various interventions and procedures by which their efficacy may be audited in each case.

Therapeutic interventions in the ICU are curative, supportive or prophylactic. The support of individual functions is a major part of intensive care, designed to buy time for natural resolution or a response to other often simpler measures. This means that it is difficult to equate the results of specific activities with outcome. Many of the most expensive and time consuming manoeuvres do no more than modulate results which are largely dictated by the nature of the underlying disease.

## Cost/benefit relationships

There are no published evaluative studies relating cost to outcome from British ICUs. Those that are available from the USA, Europe and Australia are unlikely to be applicable to the UK because of differences in case mix, quality and availability of support. Standard methods of costing in the NHS do not allow direct calculation of ICU costs. New methods of budgeting and resource management which are envisaged in the plans to develop the NHS may help to overcome this, but the information systems which would enable ICU costs to be identified precisely are not yet part of routine health service management.

To assist in our enquiry, the King's Fund and the Centre for Health Economics at York University jointly financed and conducted an exploratory study, in collaboration with three ICUs to attempt to relate, in a systematic way, data on workload, treatment, costs and outcome. The results, though not conclusive statistically, indicate that such investigations are feasible, and potentially rewarding.

*The panel recommends that priority should be given to extending this and other comparable analyses as a matter of urgency.*

## Levels of provision

Current Department of Health policy is set out in Building Note 27, originally published in 1970 and revised in 1974. This recommends that the number of beds in an ICU should be some 1 to 2% of total acute beds and that the average DGH should have an ICU with six to eight beds. According to recent surveys conducted by the Association of Anaesthetists of Great Britain and Ireland and the Medical Architecture Research Unit, most units are smaller than envisaged by the Department of Health but there is considerable variety. Those units which have fewer than four beds and which handle fewer than 200 cases per annum may be uneconomic. Such units may be undertaking too little work to provide the highest quality of care as suggested by the Association of Anaesthetists. There may be a case for concentration of intensive care provision in a smaller number of units, each of which would have a workload large enough to enable it to develop appropriate expertise.

The absence of data on workload, outcome and costs, and the heterogeneity of ICUs, make it evident that any recommendation about future provision must be highly speculative. There would appear to be a need for flexibility and for local rather than national planning. In some situations, the patient will benefit most from specialist care at Regional centres so that expensive ICU facilities would not need to be replicated in every DGH.

## Recommendations

Having carefully considered the published literature on intensive care and evidence submitted, the panel has reached the view that there is a serious lack of evidence about its costs and benefits. In part, this stems from uncertainty about who is responsible for organising and managing these services, and the consequent failure to collect data about activity and outcomes. Understandably, there has been no clinical trial of intensive care, since such a trial would present formidable practical difficulties. The absence of the economic evaluation of intensive care is much less defensible and requires urgent attention. The panel has two main recommendations.

### *Responsibility*

Each Intensive Care Unit should identify someone to be responsible for:

ensuring the unit has a clinical policy in the form of written guidelines;
ensuring that the above policies are implemented;
collecting and evaluating data on the clinical outcome and costs, in general and of the care of individual patients;
coordinating the clinical care of individual patients.

The person responsible need not necessarily be the same in each case. Conflicts may still arise despite clinical guidelines, so an independent mechanism for their resolution should be available.

### *Research*

There is an urgent need for intensivists to agree what data (clinical and economic) should be collected by every ICU to allow proper audit. Especially important is the need for prospective research to evaluate certain specific practices in intensive care. Differences between units and the variability of their practices might be used to evaluate areas of uncertainty and create hypotheses which could be tested if necessary by randomised controlled trials.

## Bibliography

Bion JF, Edlin SA, Ramsay G, McCabe S, Ledingham I M. Validation of a prognostic score in critically ill patients undergoing transport. *British Medical Journal* 1985; **291**: 432–4.

Bion JF, Wilson IH, Taylor PA. Transporting critically ill patients by ambulance: audit by sickness scoring. *British Medical Journal* 1988; **296**: 170.

Campion EW, Mulley AG, Goldstein RL, Barnett GO, Thibault GE. Medical intensive care for the elderly. A study of current use, costs and outcomes. *Journal of the American Medical Association* 1981; **246**: 2052–6.

Chang RWS, Jacobs S, Lee B. Use of Apache II severity of disease classification to identify intensive care unit patients who would not benefit from total parenteral nutrition. *Lancet* 1986; **i**: 1483–7.

Cullen DJ, Keene R, Waternaux C, Kunsman JM, Caldera DL, Peterson H. Severity of illness, outcome analysis, and cost of intensive care for critically ill patients. In: Parrillo JE, Ayres SM, eds. *Major issues in critical care medicine*. Baltimore: Williams and Wilkins, 1984.

Detsky AS, Stricker SC, Mulley AG, Thibault GE. Prognosis, survival and the expenditure of hospital resources for patients in an intensive care unit. *New England Journal of Medicine* 1981; **305:** 667–72.

Dixon R, Myers F, Rawlinson C. *Intensive therapy and coronary care units*. London: MARU, 1988.

Jennett B. Inappropriate use of intensive care. *British Medical Journal* 1984; **289:** 1709–11.

Jennett B. Decisions to limit treatment. *Lancet* 1987; **ii:** 787–9.

Knaus WA, Wagner DP, Draper EA. The range of intensive care services today. *Journal of the American Medical Association* 1981; **246:** 2711–6.

Knaus WA, Draper EA, Wagner DP, Zimmerman JE. Apache II: A severity of diseases classification system. *Critical Care Medicine* 1985; **13:** 818–29.

Knaus WA, Draper EA, Wagner DP, Zimmerman JE. An evaluation of outcome from intensive care in major medical centres. *Annals of Internal Medicine* 1986; **104:** 410–8.

Ledingham IM. Critical care medicine—reflections and projections. In: Miranda DR, Langrehr D, eds. *The ICU—a cost benefit analysis*. Amsterdam: Elsevier, 1986.

Loes O, Smith-Erichsen N, Lind B. Intensive care: cost and benefit. *Acta Anaesthesiologica Scandinavica* 1987; **84** (Suppl.): 3–19.

NIH consensus development conference statement on critical care medicine. In: Parillo JE, Ayres SM, eds. *Major issues in critical care medicine*. London: Williams and Wilkins, 1983: 277–97.

Parno JR, Teres D, Lemeshow S, Brown RB, Avrunin JS. Two-year outcome of adult intensive care patients. *Medical Care* 1984; **22:** 167–76.

Report of a working party of the Association of Anaesthetists. Provision of intensive care. London: 1988.

Ruark JE, Raffin TA. Initiating and withdrawing life support. Principles and practice in adult medicine. *New England Journal of Medicine* 1986; **318:** 25–30.

Schneiderman LJ, Spragg RJ. Ethical decisions in discontinuing mechanical ventilation. *Lancet* 1988; **318:** 984–8.

Singer DE, Carr PL, Mulley AG, Thibault GE. Rationing intensive care—physician response to a resource shortage. *New England Journal of Medicine* 1983; **309:** 1155–60.

Strauss MJ, LoGerfo JP, Yeltatzie JA, Temkin N, Hudson LD, Rationing of intensive care unit services. An everyday occurence. *Journal of the American Medical Association* 1986; **255:** 1143–6.

Teres D, Lemeshow S, Avrunin JS, Pastides H. Validation of the mortality prediction model for ICU patients. *Critical Care Medicine* 1981; **15:** 208–3.

Wagner DP, Wineland TD, Knaus WA. The hidden costs of treating severely ill patients: Charges and resource consumption in an intensive care unit. *Health Care Financing Review* 1983; **5:** 81–6.

Williams A. The cost-benefit approach to the evaluation of intensive care. In: Miranda DR, Langrehr D, eds. *The ICU—a cost benefit analysis*. Amsterdam: Elsevier, 1986.

## Appendix

*Members of the panel*

Dr J. G. G. Ledingham (Chairman of Panel), Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford; Dr P. Ashworth, Department of Nursing and Health Visiting, University of Ulster; Dr M. Branthwaite, Consultant Physician, Brompton Hospital; Professor R. G. Clark, Department of Surgery, University of Sheffield; Professor I. McA Ledingham, Department of Emergency and Critical Care Medicine, United Arab Emirates University; Dr D. Lamb, Department of Philosophy, University of Manchester; Mr A. Liddell, General Manager, East Anglia Regional Health Authority; Dr K. McPherson, Department of Community Medicine and General Practice, Radcliffe Infirmary, Oxford; Dr J. C. Stoddart, Consultant in Charge ITU, The Royal Victoria Infirmary, Newcastle upon Tyne; Mr R. Talbot, Director, Headway, National Head Injuries Association; Professor A. Williams, Institute of Research in Social Science, University of York.

*Secretariat:* Dr C. Ham, Health Policy Analyst, King's Fund Institute; Dr J. Spiby, Director, King's Fund Forum Programme.

*Anaesthesia*, 1989, Volume 44, pages 432–433

# Forum

## Possible decrease in mortality associated with anaesthesia

### A comparison of two time periods in Massachusetts, USA

G. L. Zeitlin, MD, FFARCS, Chairman, Closed Claims Study Committee, Massachusetts Society of Anesthesiologists, Senior Staff Anesthesiologist, Lahey Clinic Medical Centre, Burlington, Mass. 01805, USA.

**Summary**

*This paper compares mortality associated with anaesthesia in Massachusetts USA, during two periods of time separated by 13 years. The denominators in the calculation of the mortality rates are not precisely comparable but there appears to be approximately a thirteenfold decrease in the death rate after general anaesthesia and a tenfold decrease after spinal anaesthesia.*

**Key words**

*Statistics*; mortality rates.

This paper compares anaesthetic mortality in Massachusetts during two periods of time separated by 13 years. It compares two studies which use the technique of the community-wide mortality investigation first described by Ruth in 1945,[1] and later by the Baltimore Anesthesia Study Committee.[2]

Memery[3] published a study of anaesthesia-related deaths in a large general hospital in central Massachusetts during the period 1955–1964 and reviewed the records of all the patients anaesthetised during that period.

The Committee on Closed Claims of the Massachusetts Society of Anesthesiologists completed a study of the case files of malpractice claims against Massachusetts anaesthetists for the period 1977–1984. The majority of anaesthetists in this State are insured by a State mandated consortium of companies known as the Joint Underwriters Association (JUA). The JUA was formed in 1974 and a Committee of the Massachusetts Society of Anesthesiologists reviewed all the cases that were closed by the end of 1984. A closed claim is one that was won or lost in court or settled out of court. Our study is part of a national study by the Committee on Professional Liability of the American Society of Anesthesiologists which has led to the development of a Closed Claims database. This is a standardised collection of case summaries of over 1000 anaesthetic mishaps.[4]

Any comparison between the results of the two studies in Massachusetts suffers from some of the problems found in epidemiological investigations of mortality associated with anaesthesia:[5] but there are sufficient geographical similarities between the two groups of patients to allow some cautious conclusions to be drawn. Memery's study reported all deaths associated with anaesthesia in one large general hospital, whereas the JUA study only examines cases in which a malpractice claim was started. All the anaesthetics were given by a single group of seven anaesthetists assisted by residents in Memery's study. The JUA study pertains to approximately 300 anaesthetists who work in a variety of hospital and other settings and who supervise nurse anaesthetists and residents. It is likely that the great majority of deaths associated with anaesthesia would result in a lawsuit in the present litiginous atmosphere in the United States[6] but there is no independent evidence for this. The denominators used in the JUA study are derived and are based on, possibly unwarranted, assumptions.

### *Comparison of studies*

Memery described 69 291 anaesthetics of which 40 003 (58%) were general, 28 529 (41%) were spinal and the remainder (1%) were nerve blocks. Memery used the Baltimore Anaesthesia Study Committee criteria, to decide whether the death was related to anaesthesia. The members of that Study Committee were given data about all patients who died within 24 hours of surgery or anaesthesia. They were blinded as to the identity of the hospital, surgeon, patient or anaesthetist. They were asked, 'Did the anaesthetic management contribute to the death of the patient?', and if the answer was in the affirmative, 'Was it the principal cause?'. Memery reported 15 'anaesthesia primary' deaths giving a rate of 2.16 per 10 000 (15/69 291) anaesthetics using these criteria.

There were 31 deaths among the 151 cases of alleged malpractice in the JUA study. The study was performed by five experienced anaesthetists appointed by the Executive Committee of the Massachusetts Society of Anesthesiologists. They completed for each case a detailed eight-page questionnaire supplied by the organisers of the nationwide Closed Claims Study. The JUA involved approximately 300 anaesthetists during the first 8 years of its existence. Whitcher *et al.* (Anesthetic safety and cost effective monitoring. Scientific Exhibit, A.S.A. Annual Meeting, 1986), estimate that on average, a qualified

---

Accepted 9 November 1988.

0003–2409/89/050432 + 09 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

anaesthetist in the USA gives, or supervises 800 anaesthetics each year. The JUA study thus applies to about (8 × 300 × 800 =) 1 920 000 anaesthetics. This gives an approximate death rate of 0.16 per 10 000 (31/1 920 000) anaesthetics and suggests a thirteenfold decrease (2.16/0.16) in mortality between the two periods.

In Memery's series 28 529 patients were given a spinal anaesthetic. There were six anaesthetic deaths among these, which gives a rate of 2.1 per 10 000 (6/28 529). Nineteen (12.6%) of the 151 JUA malpractice suits resulted from the use of spinal anaesthesia. If one assumes that the number of malpractice cases is roughly proportional to the frequency of use of each method, then there were (12.6/100 × 1 920 000 =) 242 000 spinal, and (87.4/100 × 1 920 000 =) 1 678 000 general anaesthetics given in Massachusetts during the period of the JUA study. Five of the patients who received spinal anaesthesia died. This is a rate of 0.21 per 10 000 (5/242 000) and is a tenfold decrease (2.1/0.21) in the mortality rate.

### *Discussion*

In the JUA study there were another 14 cases of major or grave permanent neurological injury, which makes a total of 45 serious adverse outcomes due to anaesthesia. The Committee judged that 33 of these could have been prevented. These judgements must be interpreted cautiously. Caplan *et al.*[4] have recently demonstrated that opinions about appropriateness of care are biased by severity of outcome. The Committee also judged that 27 of these 33 preventable outcomes probably could have been prevented by the use of one or more monitoring devices. Some of these devices were not available during the 1977–1984 period and now that they are used during nearly all anaesthetics in Massachusetts[7] it is possible that there could be a further decline in mortality associated with anaesthesia, as suggested by Coté and colleagues.[8] The findings of the recently completed Confidential Enquiry into Perioperative Deaths[9] in the United Kingdom also supports such a possibility. There were only three deaths in 485 850 anaesthetics, solely because of anaesthesia.

The officials of the JUA are so convinced of the potential for a further decline in adverse outcomes due to anaesthesia that they have offered a premium discount of 20% to all the anaesthetists whom they insure in Massachusetts.[7] Anaesthetists, to qualify for this discount, must promise in writing that they will comply with the American Society of Anesthesiologists Standards for Basic Intra-operative Monitoring (*Anesthesia Patient Safety Foundation Newsletter* 1987; **2:** 3) and use a pulse oximeter on every patient and a capnometer during every anaesthetic in which it is applicable. They must also agree to random audit of compliance, by members of the Risk Management Division of the JUA.

Memery describes five of six patients who died under spinal anaesthesia to have had a high sensory level and four after supplementation with thiopentone. All five of the patients in the JUA group who died after spinal anaesthesia were noted to have had respiratory depression and cyanosis before suffering cardiac arrest. Caplan and colleagues[10] have recently described a similar group of patients and have suggested a respiratory mechanism not previously elucidated, to explain these tragedies. This suggests that oximetry and capnometry are at least as important as cardiovascular monitoring during spinal anaesthesia.

The apparent decline in death associated with anaesthesia in Massachusetts may be compared to that which occurred in New South Wales.[11] The classification of the causes of mortality in New South Wales is identical to that used in the Closed Claims Study.

Memery and his group also administered 45 575 anaesthetics in the neighbouring maternity hospital. The vast majority (97%) were spinal anaesthetics, and there were no maternal deaths. There were no maternal deaths that led to malpractice suits during the period of the JUA study. The Committee on Maternal Mortality of the Massachusetts Medical Society in 1987[12] surveyed the causes of death among 886 women who died in this state during pregnancy and within 90 days *post partum*. Their study covered the period 1954 to 1985 and happens to span the period of the two anaesthetic mortality studies compared in this paper. They give a death rate as a result of anaesthetic accident of 0.23 per 10 000 live births during the years 1954 to 1957, and 0.03 per 10 000 live births from 1982 to 1985. They do not define the term 'anaesthetic accident'.

Finally, it is worth quoting from Memery's paper, 'The mechanism of death in patients under spinal anesthesia was obvious in all but one case, in direct contrast to the mystery that frequently surrounds death in patients under general anesthesia. In view of the experience of the anesthesiologist, some of the errors committed may only be explained as human error.' He continues, 'The most frequent error was the faulty management of the anesthetic whether general or regional. The common denominator in faulty management was inadequate monitoring of the patient, and this was especially true in those deaths that occurred in good-risk patients.'

Despite the difficulties inherent in comparing mortality from anaesthesia in different groups of patients, a comparison of the only two available series in Massachusetts *suggests, but does not prove*, that there has been a substantial decline in the last 30 years.

### *References*

1. Ruth HS. Anesthesia study commissions. *Journal of the American Medical Association* 1945; **127:** 514–7.
2. Phillips OC, Frazier TM, Graff TD, Dekornfeld TJ. The Baltimore Anesthesia Study Committee. Review of 1 024 postoperative deaths. *Journal of the American Medical Association* 1960; **174:** 2015–9.
3. Memery HN. Anesthesia mortality in private practice. A ten-year study. *Journal of the American Medical Association* 1965; **194:** 1185–8.
4. Caplan RA, Posner K, Ward RJ, Cheney FW. Peer review of anesthetic mishaps: effect of severity of injury. *Anesthesiology* 1988; **69** (Suppl.): A722.
5. Derrington MC, Smith G. A review of studies of anaesthetic risk, morbidity and mortality. *British Journal of Anaesthesia* 1987; **59:** 815–33.
6. Huber PW. *Liability; the legal revolution and its consequences.* New York: Basic Books, 1988.
7. Zeitlin GL, Cass WA, Gessner JS. Insurance incentives and the use of monitoring devices. *Anesthesiology* 1988; **69:** 441.
8. Coté CJ, Goldstein EA, Coté MA, Hoaglin DC, Ryan JF. A single-blind study of pulse oximetry in children. *Anesthesiology* 1988; **68:** 184–8.
9. Buck N, Devlin HS, Lunn JN. *Report of the confidential enquiry into perioperative deaths.* London: Nuffield Provincial Hospitals Trust and the King's Fund for Hospitals, 1987.
10. Caplan RA, Ward RJ, Posner K, Cheney FW. Unexpected cardiac arrest during spinal anesthesia: a closed claims analysis of predisposing factors. *Anesthesiology* 1988; **68:** 5–11.
11. Holland R. Anaesthetic mortality in New South Wales. *British Journal of Anaesthesia* 1987; **59:** 834–41.
12. Sachs BP, Brown DAJ, Driscoll SG, Schulman E, Acker D, Ransil BJ, Jewett JF. Maternal mortality in Massachusetts. Trends and prevention. *New England Journal of Medicine* 1987; **316:** 667–72.

*Anaesthesia*, 1989, Volume 44, pages 434–436

# Spinal anaesthesia in infants born prematurely

T. M. Gallagher, MD, MRCPI, FFARCSI, P. M. Crean, MB, FFARCSI, Consultant Paediatric Anaesthetists, Royal Belfast Hospital for Sick Children, Belfast, BT12 6BE.

## Summary

*Spinal anaesthesia was used for 25 infants who were born prematurely and who subsequently required inguinal herniotomy. Hyperbaric bupivacaine 0.5% was administered in a dose of 0.3 mg/kg. Satisfactory surgical anaesthesia was achieved in 22 patients and there were no episodes of haemodynamic instability. The technique was not associated with postoperative apnoea. Spinal anaesthesia is a safe and effective alternative to general anaesthesia in these high-risk infants. However, postoperative apnoea monitoring is still essential for all infants born prematurely.*

## Key words

*Anaesthetic techniques*; spinal.
*Anaesthesia*; paediatric.

The development of life-threatening apnoea after general anaesthesia and surgery is more likely in infants born prematurely than in term infants.[1] Apnoea may occur up to a postconceptual age of 60 weeks[2] with reported incidences of 18%,[1] 21%[3] and 37%.[2] It has been suggested that some of the problems associated with general anaesthesia in these patients may be avoided by the use of spinal anaesthesia.[4] The present study was undertaken to evaluate spinal anaesthesia in infants who were born prematurely and who required inguinal herniotomy. The local anaesthetic administered was hyperbaric bupivacaine 0.5% which has not been used previously in such infants.

### *Methods*

Twenty-five infants born at less than 37 weeks' gestational age and who subsequently required inguinal herniotomy were studied. Eleven patients required mechanical ventilation at birth and five of these had bronchopulmonary dysplasia at the time of surgery. The mean gestational age at birth was 30 weeks. The mean weight of these infants at the time of surgery was 3.0 kg and the mean postconceptual age was 41 weeks (Table 1).

A milk feed was allowed 6 hours pre-operatively and clear oral fluids up to 2 hours before surgery. An intravenous infusion of 0.18% saline in 4% dextrose was started, at a rate of 4 ml/kg/hour after arrival of the child in the operating theatre. Monitoring included a precordial stethoscope, electrocardiogram, indirect arterial pressure with a Dinamap 845 Vital Signs Monitor, pulse oximetry and temperature measurement. Intravenous atropine 0.02 mg/kg was administered and the infant was turned to the lateral position with the back flexed and the chin extended. Lumbar puncture was carried out at the $L_{4-5}$ or $L_5/S_1$ interspace, using the hollow stilette of a 24-gauge cannula or a 25-gauge lumbar puncture needle. A tuberculin syringe that contained the appropriate volume of heavy plain bupivacaine 0.5% was attached to the needle after free-flowing cerebrospinal fluid had been obtained. A volume of 0.05–0.1 ml of cerebrospinal fluid was aspirated immediately before injection to ensure correct placement of the needle. The local anaesthetic was injected over a 10-second period; a second aspiration was performed during injection to ensure continued correct placement of the needle. The volume of hyperbaric bupivacaine 0.5% administered was based on the formula: 0.06 ml/kg + 0.1 ml. The infant was turned to the supine position after the procedure.

The spinal block was regarded as successful if there was almost immediate loss of tone in the lower limbs. Ketamine 1 mg/kg was given intravenously if the infant was restless. Loose restraints were applied to the infant's upper limbs to prevent undue movement, and surgery was started. Heart rate and indirect arterial pressure were measured at 2-minute intervals during the procedure. Postoperative monitoring with an MR 10 apnoea alarm was carried out for 24 hours.

### *Results*

Satisfactory surgical conditions were achieved in 22 patients. Four of these infants received 1.0 mg/kg ketamine because of restlessness. General anaesthesia was required in three patients (Table 2).

There were no hypotensive episodes during surgery and systolic arterial pressure and heart rate remained largely unchanged from control values (Table 3). There were no episodes of apnoea intra- or postoperatively.

### *Discussion*

Our findings suggest that spinal anaesthesia is a useful and suitable alternative to general anaesthesia in infants born prematurely. Three failures occurred early in the series and were due to technical difficulties in performance of the block; this is comparable to the failure rate reported in other series.[4–7] There is no doubt that increased experience leads to a higher rate of successful block. The main

Accepted 1 December 1988.

**Table 1.** Clinical data.

| Patient | Gestational age (weeks) | Post-conceptual age (weeks) | Weight at time of surgery (kg) | Perinatal treatment | Residual problems |
|---|---|---|---|---|---|
| 1 | 36 | 40 | 3.2 | | |
| 2 | 30 | 38 | 2.2 | O$_2$, antibiotics | |
| 3 | 32 | 52 | 4.6 | O$_2$, antibiotics | BPD |
| 4 | 30 | 42 | 2.5 | IPPV, O$_2$, surfactant, antibiotics | BPD |
| 5 | 28 | 40 | 3.2 | IPPV, O$_2$, antibiotics | |
| 6 | 28 | 44 | 2.9 | IPPV, O$_2$, antibiotics | |
| 7 | 35 | 44 | 3.4 | | BPD |
| 8 | 32 | 44 | 4.1 | Surfactant | |
| 9 | 35 | 40 | 3.8 | | |
| 10 | 29 | 50 | 4.2 | IPPV, O$_2$, antibiotics | |
| 11 | 28 | 40 | 3.1 | IPPV, O$_2$, antibiotics | |
| 12 | 34 | 46 | 4.7 | | |
| 13 | 33 | 40 | 2.1 | | BPD |
| 14 | 27 | 40 | 1.8 | IPPV, O$_2$, antibiotics, steroids | |
| 15 | 27 | 41 | 2.8 | IPPV, O$_2$, antibiotics | BPD |
| 16 | 28 | 38 | 2.4 | IPPV, O$_2$, antibiotics | |
| 17 | 35 | 44 | 3.4 | | |
| 18 | 28 | 42 | 1.8 | IPPV, O$_2$, antibiotics | |
| 19 | 30 | 42 | 2.4 | | |
| 20 | 27 | 39 | 3.2 | Surfactant, IPPV, O$_2$, antibiotics | |
| 21 | 31 | 35 | 2.3 | O$_2$, antibiotics | |
| 22 | 34 | 40 | 2.8 | | |
| 23 | 32 | 42 | 3.0 | | |
| 24 | 28 | 45 | 3.0 | IPPV, O$_2$, antibiotics | |
| 25 | 35 | 41 | 2.9 | | |
| Mean (SD) | 30.8 (3.0) | 41.9 (3.7) | 3.0 (0.8) | | |

BPD, bronchopulmonary dysplasia; IPPV, intermittent positive pressure ventilation.

**Table 2.** Results of spinal anaesthesia in 25 infants born prematurely.

| | |
|---|---|
| Successful spinals | 22 |
| Unsuccessful spinals | 3 |
| Number who required ketamine | 4 |
| Complications | 0 |

**Table 3.** Cardiovascular measurements. Data are presented as mean (SD).

| | Before atropine | Before spinal | 5 minutes | 10 minutes | 15 minutes |
|---|---|---|---|---|---|
| Heart rate, beats/minute | 145 (11) | 164 (15) | 162 (12) | 160 (12) | 162 (10) |
| Systolic arterial pressure, mmHg | 84 (5) | 80 (4) | 78 (5) | 80 (6) | 82 (5) |

difficulties with the use of spinal anaesthesia are identification of the subarachnoid space and injection of the drug.[4–6] The hollow stilette of a 24-gauge intravenous cannula was used in the earlier cases but latterly a 25-gauge lumbar puncture needle became available and is now used routinely. It is important to aspirate 0.05–0.1 ml of cerebrospinal fluid to ensure correct placement of the needle before injection of the local anaesthetic.[8] The lumbar puncture should be performed at or below the L$_{4-5}$ interspace in order to avoid damage to the neonatal spinal cord, which may extend as far as L$_4$. Undue flexion of the cervical spine should also be avoided since this may be associated with arterial desaturation.[9]

Ketamine was administered to four patients because of restlessness and was not associated with any cardiovascular or respiratory disturbance. The other patients either slept during the surgical procedure or were soothed easily with a pacifier.

Hyperbaric bupivacaine 0.5% has been investigated extensively as a spinal anaesthetic agent in adults and produces consistently good operating conditions.[10,11] Blaise and Roy[5] have reported its use as a spinal anaesthetic agent in infants and older children, but there are no previous reports of its use in infants born prematurely. Hyperbaric amethocaine, which is comparable in terms of potency and toxicity,[12,13] was used in previous studies of spinal anaesthesia in these high risk patients. In the present series, bupivacaine was administered in a dose of 0.3 mg/kg, which is equivalent to the dose of amethocaine recommended by Abajian *et al.*[4] It has been suggested[7,14] that infants who weigh less than 2 kg may need a higher dose of local anaesthetic agent, but our experience suggests that bupivacaine 0.3 mg/kg provides satisfactory surgical conditions. More recently, higher doses of bupivacaine in a plain solution have been used but appear to be associated with a greater incidence of cardiovascular complications.[15]

No formal attempt was made to estimate the duration of sensory blockade in the present study. Motor function was restored fully within 75 minutes, a finding which has been reported by others.[5,7,14,15] This short duration of action in infants may be due to a lower concentration of the drug in the cerebrospinal fluid[4] and to physical and physiological differences in the central nervous system of infants and of adults.[16]

It was extremely difficult to establish the upper level of anaesthesia since the various tests traditionally used in adult practice may be unreliable.[17] A peripheral nerve stimulator adjusted to produce tetanic stimulation and thus to induce a withdrawal response,[14] and the effect of pinprick,[15] were used to identify the level of cutaneous analgesia. However, we found that the almost immediate loss of tone in the lower limbs after spinal blockade was a clinically reliable sign of satisfactory surgical anaesthesia.

Cardiovascular stability was maintained during spinal anaesthesia;[4,7,14] changes of less than 10% occurred in heart rate and systolic arterial pressure. This contrasts with reports in adults, in whom a decrease of 15–20% may occur in blood pressure during spinal blockade.[11] An immature sympathetic nervous system in the infant may account for this difference.[7]

Preterm infants are prone to develop apnoea because of immaturity of the central nervous system,[18] and general anaesthesia may aggravate this tendency further. Halothane depresses the chemoreceptor response to hypoxaemia and hypercapnia[19] and the residual effects of relaxants and opioids may decrease central respiratory drive further.[20] Other problems associated with general anaesthesia include the risk of aspiration, atelectasis and extubation stridor. It is perhaps not unexpected that some of these infants develop apnoea after general anaesthesia, and that a proportion may require mechanical ventilation.[3] There were no episodes of apnoea in the present series, although Harnik *et al.*[7] have reported apnoea after spinal anaesthesia in a prematurely born infant who became hypothermic. The incidence of apnoea appears to be lower after spinal than general anaesthesia; nevertheless, apnoea monitoring is essential for at least 12 hours postoperatively.[2]

The findings of this study support the views of those who advocate spinal anaesthesia for infants born prematurely, who require inguinal herniotomy. It is a safe and effective alternative to general anaesthesia and is rarely associated with apnoea. Hyperbaric bupivacaine 0.5% in a dose of 0.3 mg/kg is a suitable anaesthetic agent and produces satisfactory surgical conditions. Postoperative apnoea monitoring for an appropriate period is always necessary in infants born prematurely, irrespective of the anaesthetic technique.

## *Acknowledgment*

We are most grateful to Mrs E. Archer and Mrs M. O'Reilly who provided excellent secretarial assistance.

## *References*

1. STEWARD DJ. Preterm infants are more prone to complications following minor surgery than are term infants. *Anesthesiology* 1982; **56**: 304–6.
2. KURTH CD, SPITZER AR, BROENNLE AM, DOWNES JJ. Postoperative apnea in preterm infants. *Anesthesiology* 1987; **66**: 483–8.
3. LIU LMP, COTE CJ, GOUDSOUZIAN NG, RYAN JF, FIRESTONE S, DEDRICK DF, LIU PL, TODRES ID. Life-threatening apnea in infants recovery from anesthesia. *Anesthesiology* 1983; **59**: 506–10.
4. ABAJIAN JC, MELLISH RWP, BROWNE AF, PERKINS FM, LAMBERT DH, MAZUZAN JE. Spinal anesthesia for surgery in the high-risk infant. *Anesthesia and Analgesia* 1984; **63**: 359–62.
5. BLAISE GA, ROY WL. Spinal anaesthesia for minor paediatric surgery. *Canadian Anaesthetists' Society Journal* 1986; **33**: 227–30.
6. JUNKIN CI. Spinal anaesthesia in children. *Canadian Medical Association Journal* 1933; **26**: 51–3.
7. HARNIK EV, HOY GR, POTOLICCHIO S, STEWART DR, SIEGELMAN RE. Spinal anesthesia in premature infants recovering from respiratory distress syndrome. *Anesthesiology* 1986; **64**: 95–9.
8. SINGLER RC. Pediatric regional anesthesia. In: GREGORY GA, ed; *Pediatric anesthesia*. New York: Churchill Livingstone, 1983: 481–518.
9. GLEASON CA, MARTIN RJ, ANDERSON JV, CARLO WA, SANNITI KJ, FANAROFF AA. Optimal position for a spinal tap in preterm infants. *Pediatrics* 1983; **71**: 31–5.
10. CHAMBERS WA, LITTLEWOOD DG, EDSTROM HH, SCOTT DB. Spinal anaesthesia with hyperbaric bupivacaine: effects of concentration and volume administered. *British Journal of Anaesthesia* 1982; **54**: 75–80.
11. CHAMBERS WA, EDSTROM HH, SCOTT DB. Effect of baricity on spinal anaesthesia with bupivacaine. *British Journal of Anaesthesia* 1981; **53**: 279–82.
12. HENN F, BRATTSAND R. Some pharmacological and toxicological properties of a new long-acting local analgesic, LAC-43 (Marcaine$^{(R)}$) in comparison with mepivacaine and tetracaine. *Acta Anaesthesiologica Scandinavica* 1966; **21**(Suppl.): 9–30.
13. PFLUG AE, AASHEIM GM, BECK HA. Spinal anesthesia: bupivacaine versus tetracaine. *Anesthesia and Analgesia* 1976; **55**: 489–92.
14. RICE L, DEMARS P, CROOMS J, WHALEN T. Duration of spinal anesthesia in infants under one year of age: comparison of three drugs. *Anesthesia and Analgesia* 1987; **66**: S148.
15. MAHE V, ECOFFEY C. Spinal anesthesia with isobaric bupivacaine in infants. *Anesthesiology* 1988; **68**: 601–3.
16. DOHI S, NAITO J. TAKAHASHI T. Age-related changes in blood pressure and duration of motor block in spinal anesthesia. *Anesthesiology* 1979; **50**: 319–23.
17. BERKOWITZ S, GREENE BA. Spinal anesthesia in children; report based on 350 patients under 13 years of age. *Anesthesiology* 1951; **12**: 376–87.
18. HENDERSON-SMART DJ, PETTIGREW AG, CAMPBELL DJ. Clinical apnea and brain-stem neural function in preterm infants. *New England Journal of Medicine* 1983; **308**: 353–7.
19. KNILL RL, GELB AW. Ventilatory responses to hypoxia and hypercapnia during halothane sedation and anesthesia in man. *Anesthesiology* 1978; **49**: 244–51.
20. GREGORY GA, STEWARD DJ. Life-threatening perioperative apnea in the ex-'premie'. *Anesthesiology* 1983; **59**: 495–8.

*Anaesthesia*, 1989, Volume 44, pages 437–440

# Daycase anaesthesia and anxiety

## A study of anxiety profiles amongst patients attending a Day Bed Unit

J. W. Mackenzie,* MRCP, FFARCS, Registrar in Anaesthetics and Intensive Care, Royal Berkshire Hospital, Reading RG1 5AN.

### Summary

*Two hundred adult patients aged 16–65 years scheduled to undergo operation under general anaesthesia in a Day Bed Unit were assessed for anxiety at the time of booking and on the day of operation. The nature of previous anaesthetic experience was the prime determinant of the anxiety scores obtained at booking. The score at booking was the prime determinant of the score on the day of operation, with previous experience and type of operation as secondary independent factors. Patients scheduled to undergo oral surgery were particularly anxious. Nineteen percent of patients would have liked to have received something to relieve their anxiety.*

**Key words**

*Anaesthesia*; outpatient.
*Anxiety*; pre-operative.

This study was undertaken to assess indices of anxiety amongst patients who attended the Day Bed Unit (DBU) of a District General Hospital. There is little published work on this subject. Male[1] found low levels of anxiety in day surgery patients, and reported that general anaesthesia rather than local anaesthesia, and male gender, were associated with a low anxiety score.

The purpose of this study was to define anxiety levels in our patient population and attempt to identify any subgroup of patients in whom indices of anxiety were elevated.

### *Method*

The study was carried out over a 3-month period when adults aged 16–65 years scheduled for operation under general anaesthesia were invited to take part in the study at the time they booked their operation in the DBU.

All patients were prepared in the normal way; their queries were answered and attempts made to allay common concerns before they were invited to take part in the study.

**Table 1.** Questions asked at time of booking.

Have you ever had an anaesthetic in the past/been put to sleep for an operation?
If yes, was this an unpleasant experience?
Are you worried by the operation?
Are you worried by the anaesthetic?

**Table 2.** The Multiple Affect Adjective Check List (MAACL).[2]

| | | | |
|---|---|---|---|
| Afraid | Nervous | Calm | Joyful |
| Fearful | Panicky | Cheerful | Pleasant |
| Desperate | Shaky | Contented | Thoughtful |
| Frightened | Tense | Loving | Steady |
| Terrified | Worrying | Happy | Secure |
| Upset | | | |

Seventy-six percent of those invited agreed to take part (9% of patients who presented for surgery were not approached to join the study because of pressure of routine work on the day of booking). The patients were given a brief questionnaire to complete. Their proposed date of operation was recorded and a second questionnaire was included with their notes in readiness for their day of operation. The same patients were thus assessed on two occasions; on the day of booking their operation, and on the actual day of operation before going to theatre. However, 19 were unable to complete the second questionnaire because of lack of time before operation.

Four questions (Table 1) were asked at the time of booking. The age and sex of the patient, and the type of operation, were noted, and anxiety was assessed (see below).

Questions 3 and 4 were repeated on the day of operation, and a check made that no anaesthetic had been administered in the interim. A final question, preceded by an explanation of why premedication is not given, asked: would you have liked to have received something to make you feel more relaxed?

Anxiety was assessed in two ways. A visual analogue scale was presented to the patient. One end of the horizontal 10-cm line was labelled 'not at all worried', and the other end 'absolutely terrified'. In addition, a modification of the Multiple Affect Adjective Check List (MAACL) was used.[2] This contained 11 'anxious' and 10 'calm' words (Table 2) which the subject viewed, and circumscribed the word or words which he (she) considered to represent his (her) feelings at the time of assessment. The MAACL score is calculated from the sum of the 'anxious' word score (score 1 for each 'anxious' word ringed) plus the 'calm' word score (score 1 for every calm word rejected i.e. 10 − number of 'calm' words ringed). Thus the score can range from 0 to 21; the higher the score the more anxious is the subject.

---

* Present address, Senior Registrar, Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford OX2 6HE.

Accepted 28 November 1988.

**Table 3.** Age and visual analogue scale (VAS) scores. Data are presented as mean (95% confidence intervals).

| | Age (years) | Day of booking VAS (mm) | Day of operation VAS (mm) |
|---|---|---|---|
| All patients | 31.4 | 40.5 | 46.7 |
| ($n$ = 164) | (29.9–32.9) | (35.8–45.2) | (42.4–51.0) |
| All women | 31.3 | 42.3 | 48.6 |
| ($n$ = 143) | (29.6–33.0) | (37.2–47.4) | (44.0–53.2) |
| All men | 31.9 | 28.6 | 34.0 |
| ($n$ = 21) | (30.1–35.7) | (16.5–40.7) | (22.9–45.1) |
| Gynaecology | 34.3 | 36.3 | 44.4 |
| ($n$ = 77) | (32.3–36.3) | (38.5–42.6) | (38.5–50.3) |
| Breast lumpectomy | 32.5 | 48.5 | 53.1 |
| ($n$ = 13) | (26.5–38.5) | (31.2–65.8) | (38.4–67.8) |
| General surgery | 35.6 | 29.0 | 30.8 |
| ($n$ = 25) | (31.1–40.1) | (18.3–39.7) | (21.9–39.7) |
| Oral surgery | 24.7 | 50.9 | 56.9 |
| ($n$ = 49) | (22.7–26.7) | (43.7–60.1) | (48.9–64.9) |

**Table 4.** Multiple affect adjective check list (MAACL) scores. Data are presented as mean (95% confidence intervals).

| | Day of booking MAACL | Day of operation MAACL |
|---|---|---|
| All patients | 11.0 | 11.4 |
| ($n$ = 164) | (10.7–11.3) | (11.1–11.7) |
| All women | 11.1 | 11.6 |
| ($n$ = 143) | (10.8–11.4) | (11.2–12.0) |
| All men | 10.1 | 10.2 |
| ($n$ = 21) | (9.2–11.0) | (9.5–10.9) |
| Gynaecology | 10.9 | 11.2 |
| ($n$ = 77) | (10.5–11.3) | (10.8–11.6) |
| Breast lumpectomy | 11.5 | 11.5 |
| ($n$ = 13) | (10.2–12.8) | (10.4–12.6) |
| General surgery | 10.4 | 10.8 |
| ($n$ = 25) | (9.5–11.3) | (10.1–11.5) |
| Oral surgery | 11.3 | 11.8 |
| ($n$ = 49) | (10.6–12.0) | (10.9–12.7) |

**Table 5.** Nurses' assessment of patient demeanour on day of booking.

| | Not anxious | Anxious | Very anxious |
|---|---|---|---|
| No. of patients | 58 | 41 | 7 |
| Mean age in years | 32.7 | 29.5 | 32.9 |
| (95% confidence interval) | (30.1–35.3) | (26.8–32.2) | (26.3–39.5) |
| Mean VAS in mm | 26.8 | 54.4 | 76.4 |
| (95% confidence interval) | (20.0–33.6) | (46.6–59.2) | (56.8–96.0) |
| Mean MAACL | 10.0 | 11.8 | 13.1 |
| (95% confidence interval) | (9.5–10.5) | (11.5–12.7) | (11.3–14.9) |

**Table 6.** Nurses' assessment of patient demeanour on day of operation.

| | Not anxious | Anxious | Very anxious |
|---|---|---|---|
| No. of patients | 73 | 47 | 13 |
| Mean age in years | 32.0 | 32.3 | 28.0 |
| (95% confidence interval) | (29.6–34.4) | (29.2–35.4) | (24.0–32.0) |
| Mean VAS in mm | 35.7 | 55.0 | 92.3 |
| (95% confidence interval) | (30.2–41.2) | (47.9–62.1) | (88.5–96.1) |
| Mean MAACL | 10.8 | 12.1 | 13.2 |
| (95% confidence interval) | (10.3–11.3) | (11.5–12.7) | (11.8–14.6) |

**Table 7.** Anxiety scores on day of operation in relation to previous anaesthetic experience.

| | None | Bad | Good |
|---|---|---|---|
| No. of patients | 40 | 33 | 91 |
| Mean age in years | 26.5 | 33.5 | 32.8 |
| (95% confidence interval) | (24.2–28.8) | (29.5–37.5) | (30.8–34.8) |
| Mean VAS in mm | 61.2 | 53.0 | 38.2 |
| (95% confidence interval) | (52.8–69.6) | (43.8–63.2) | (33.0–43.4) |
| Mean MAACL | 12.0 | 12.0 | 11.1 |
| (95% confidence interval) | (11.3–12.7) | (11.2–12.8) | (10.6–11.6) |

Independently (i.e. without looking at the patient's responses), the DBU nurses were asked to estimate the patient's demeanour on a three-point scale (not anxious/anxious/very anxious) which they added to the completed questionnaire.

The MAACL scores were found to be distributed normally; the VAS scores conformed to a normal distribution following logarithmic transformation. Statistical analysis was with paired or unpaired $t$-tests as appropriate with checks on the variance ratio beforehand. The scores of the female patients were subjected to multiple regression analysis in an attempt to identify which variable or variables provided the best prediction of heightened anxiety.

### *Results*

One hundred and eighty-one of the 200 questionnaires distributed originally were retrieved on the day of operation. Of these, 17 could not be included in the analysis due to incomplete or unintelligible data. Thus, 164 questionnaires were examined. One hundred and forty-three (86%) of the patients with complete records were female. Table 3 shows the ages, types of operation and VAS assessments for all patients. The MAACL results are shown in Table 4.

Overall, both anxiety scores on the day of operation exceeded those on the day of booking ($p < 0.01$). Scores for males and females were not significantly different on the day of booking but a highly significant difference (female scores > male) was identified in both VAS and MAACL on the day of operation ($p < 0.01$). The type of operation associated with highest anxiety scores was oral surgery even though 26% of patients were male.

The age distributions (Table 3) of the male and female patients were similar, although the mean age of patients who underwent oral surgery was a decade younger than that of the other surgical groups.

The nurses assessed 106 patients on the day of booking and 133 on the day of operation (Tables 5 and 6). Their assessments correlated well with the VAS results, and less well with MAACL scores.

Anxiety scores on the day of operation were examined to assess the effect of previous anaesthetic experience (satisfactory previous anaesthetic experience, unpleasant previous experience or no previous anaesthetic experience). These data are presented in Table 7. Individuals with no previous anaesthetic experience or previously unpleasant experience had greater anxiety scores than those with previously satisfactory anaesthetic experience. Patients with no previous anaesthetic experience were younger than those in the other two groups but there was no bias in distribution of the sexes.

Figures 1 and 2 show the VAS and MAACL scores in each age band on the day of operation. There was a trend

**Table 8.** Principal cause of concern on day of operation in relation to anxiety scores.

| | Operation | Anaesthetic | Neither | Both |
|---|---|---|---|---|
| No. of patients | 44 | 37 | 21 | 62 |
| Mean age in years (95% confidence interval) | 27.6<br>(25.2–29.0) | 32.8<br>(32.0–35.6) | 40.9<br>(36.7–45.1) | 30.9<br>(28.3–33.5) |
| Mean VAS in mm (95% confidence interval) | 37.7<br>(30.9–44.5) | 43.1<br>(35.9–50.3) | 15.0<br>(9.6–20.4) | 65.6<br>(59.6–71.6) |
| Mean MAACL (95% confidence interval) | 10.9<br>(10.3–11.5) | 11.4<br>(10.8–12.0) | 9.3<br>(8.7–9.9) | 12.4<br>(11.9–12.9) |

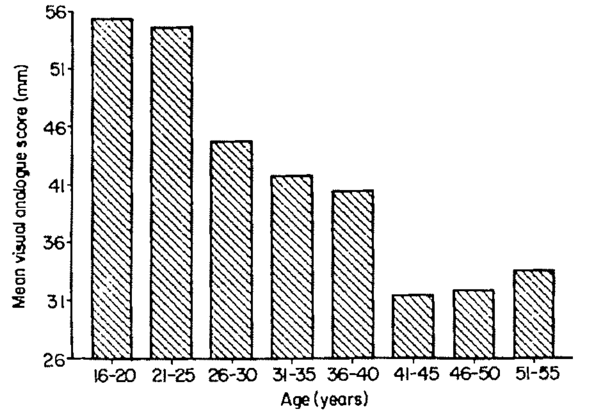


**Fig. 1.** Relationship between age and visual analogue anxiety scores on the day of operation.

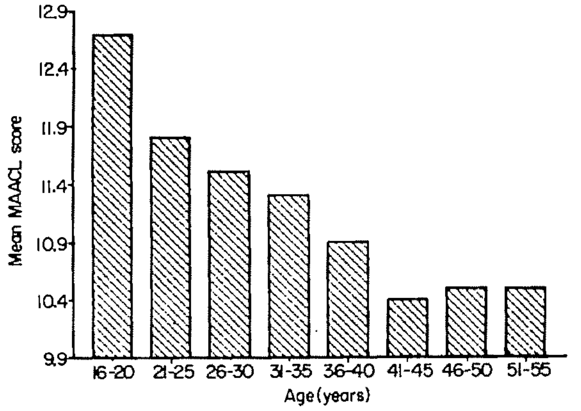


**Fig. 2.** Relationship between age and multiple affect adjective check list (MAACL) on the day of operation.

**Table 9.** Day of operation anxiety scores and premedication request.

| | Requesters | Decliners |
|---|---|---|
| No. of patients | 32 | 132 |
| Mean age in years (95% confidence interval) | 30.9<br>(27.5–34.1) | 31.2<br>(29.5–32.9) |
| Mean VAS in mm (95% confidence interval) | 68.8<br>(59.0–78.6) | 43.2<br>(38.4–48.0) |
| Mean MAACL (95% confidence interval) | 12.6<br>(11.8–13.4) | 11.2<br>(10.8–11.6) |

that suggested reduced anxiety in older patients. This relationship was examined further by one-way analysis of variance, and an effect of age was confirmed on both day of booking and day of operation. However, multiple regression analysis identified that chronological age is not the prime determinant of the scores obtained in this study.

Patients were invited to express their prime concern on the day of operation. Their replies can be summarised as the operation, the anaesthetic, both or neither. The anxiety scores and ages of those who gave each response are shown in Table 8. There was no significant difference between the anxiety scores obtained from those citing anaesthesia rather than operation as the main cause of concern. There was no relationship between the quality of previous anaesthetic experience and selection of 'anaesthesia' as the prime concern. Patients who were concerned by neither anaesthetic nor the operation had lower anxiety scores than those who expressed a concern, and were older. Thirty-one percent of those patients scheduled for excision of a breast lump were concerned primarily with the operation.

Thirty-two patients (19%) indicated that they would have liked an anxiolytic premedication (Table 9). The differences in anxiety scores between those who would have liked premedication and those who have declined it were significant ($p < 0.01$). Twenty-nine of the 32 (91%) were female but this proportion does not differ from that of the remainder (94%). However, 23/32 expressed both operation and anaesthetic as prime concerns whereas only 39 of the remaining 132 were worried by both; this difference is highly significant ($p < 0.001$). There was no difference between these 32 patients and the remainder in respect of the quality of previous anaesthetic.

A general linear interactive modelling package was used to examine how well the variables age, type of operation and previous anaesthetic experience could account for the anxiety scores obtained from the 143 female patients on the two occasions. Each variable was entered into the model and a test of significance carried out; this process was repeated until all combinations and sequences of variables had been examined, and the best fit identified for both VAS and MAACL scores. The best fit on the day of booking was a simple linear model based on previous anaesthetic experience, i.e. the quality of the patient's previous anaesthetic experience (none, bad or good) was the prime determinant of the anxiety scores. The model on the day of operation was very similar, as both indices of anxiety were determined primarily by the scores on the day of booking. However, previous anaesthetic experience and type of operation also influenced these scores. Age was a lesser determinant of the MAACL scores only.

## *Discussion*

This study has examined the inter-relationship of a number of factors which contribute to heightened anxiety in day stay patients. During the study it became apparent that the MAACL could have been made more sensitive if the words had been presented one at a time, as many patients chose only one word from the whole list. This may be responsible for the fact that the MAACL scores appeared to be less discriminatory than the VAS scores in relation to previous anaesthetic experience. The four recovery ward nurses were able to score anxiety on a three-point scale, and their assessments correlated well with those from VAS and MAACL; this is in contrast with the findings of Male.[1]

Anxiety scores were greater in female patients than in males. There was a large proportion of female patients in the study; this tended to increase the apparent anxiety profile of the study population, but reflects the fact that many day stay patients in the United Kingdom undergo minor gynaecological procedures.

There was a significant effect of type of operation on anxiety score. This effect is probably composite, and influenced by the sex bias, and lack of previous anaesthetic experience in younger patients. There were more patients with no previous anaesthetic experience in the oral surgery group (45% compared with 12–17% in other operative groups). Anxiety scores of the 'novices' were greater than those of 'experienced' patients. Those with previously unpleasant experience displayed more anxiety than those who had had an uneventful experience.

As might be expected, those with no previous anaesthetic experience were younger, and age was related inversely to anxiety scores. There was no significant difference in age distribution between the sexes, but patients in the oral surgical group were younger than those in the other three groups.

Young age and no previous anaesthetic experience commonly coexist and thus these variables have a confounding effect on each other. However, the multiple regression analysis demonstrated that experience exerted a greater influence on anxiety at booking and on the day of operation. Increasing age appeared to be related to the likelihood of acquiring good anaesthetic experience.

It is interesting that although 'bad' or 'no previous' anaesthetic experience were associated so strongly with heightened anxiety, 'anaesthesia' was not cited more frequently as a principal concern among these individuals.

Those patients who would have liked to have been given an anxiolytic premedicant (19%) were almost all concerned about both the anaesthetic and the operation. Male[1] found that 14% of patients would have liked premedication but was unable to demonstrate a significant difference in anxiety scores between these patients and those who declined premedication.

Premedication is traditionally withheld for day stay patients so as to promote early ambulation and fitness to return home.[3] A number of studies have shown temazepam[4,5] and triazolam[6] to be suitable in day stay patients, but these drugs are not used routinely. This study has identified a clear desire for premedication in 19% of patients who underwent day stay procedures.

The anxiety scores at booking were the prime determinants of the scores on the day of operation. Thus, anxiety detected at the time of booking could alert medical staff to the need for reassurance, and if necessary anxiolytic premedication, on the day of operation. Trained nurses could identify anxious patients. In addition, patients with no previous or bad anaesthetic experience can be identified easily and might also benefit from relief of anxiety.

Quality of previous anaesthetic experience should be noted during any study of anxiety related to anaesthesia or surgery to ensure that no difference exists between control and study groups. The present study was carried out on daycase patients, but many of the findings will be relevant to inpatients who exhibit heightened anxiety.

## *Acknowledgments*

The author thanks Sister E. Heading and her staff for their assistance in the collection of the data, and Dr T.B. Boulton for his helpful comments and encouragement. Thanks are due also to Dr J. Whitehead and students at the Department of Applied Statistics, University of Reading for performing the multiple regression analysis. The author was awarded the Mitchell Prize (Oxford Region) in February 1988 for a preliminary report on this topic before the results of the multiple regression analysis were available.

## *References*

1. MALE CG. Anxiety in day surgery patients. *British Journal of Anaesthesia* 1981; **53:** 663P.
2. ZUCKERMAN M. The development of an affect adjective check list for the measurement of anxiety. *Journal of Consulting Psychology* 1960; **24:** 457–62.
3. ADAMS AK. Psychological preparation and premedication. In: GRAY TC, NUNN JF, UTTING JE, eds. *General anaesthesia*, 4th edn. London: Butterworths, 1980: 909–21.
4. GREENWOOD BK, BRADSHAW EG. Preoperative medication for daycase surgery. A comparison between oxazepam and temazepam. *British Journal of Anaesthesia* 1983; **55:** 933–6.
5. BEECHEY APG, ELTRINGHAM RJ, STUDD C. Temazepam as premedication in day surgery. *Anaesthesia* 1981; **36:** 10–5.
6. THOMAS D, TIPPING T, HALIFAX R, BLOGG CE, HOLLANDS MA. Triazolam premedication. A comparison with lorazepam and placebo in gynaecological patients. *Anaesthesia* 1986; **41:** 692–7.

Anaesthesia, 1989, Volume 44, pages 441–443

SPECIAL ARTICLE

# Report of a meeting of the International Committee for Prevention of Anesthesia Mortality and Morbidity

J. B. Cooper, Associate Professor of Anesthesia, Harvard Medical School, and Director of Anesthesia Technology, Massachusetts General Hospital, Boston, Mass. 02114, USA.

A meeting of this discussion group (ICPAMM) was held on 22 May 1988 in Washington, DC. There were 61 invited participants who represented 19 countries informally. ICPAMM is a communication network among individuals who are involved in the study of anaesthesia mortality and morbidity and related issues or who are involved in the creation or the implementation of policies aimed at anaesthesia patient safety. The primary objective of this meeting was to review recent studies with emphasis on experimental methods. Presenters were asked to share experiences about the relatively successful and the not so successful aspects of their investigations.

Six studies were described: the Confidential Enquiry into Perioperative Deaths (United Kingdom),[1] a randomised trial of four anaesthetic regimens (USA/Canada), the analysis of malpractice closed claims (USA),[2] a prospective critical incident survey (Australia), the Manitoba Study (Canada)[3] and the recovery-room-impact events study (USA).[4] It became clear in the course of discussions that the study of anaesthetic outcomes has become of intense interest in the anaesthesia communities of many countries. Patient safety is high on the agenda of research and clinical interests.

The presentations of investigations illustrated the spectrum of anaesthesia outcomes and the ways that they can be studied. Dr J.N. Lunn described how CEPOD reviewed reports of deaths within 30 days of a half million operations in three regions of the United Kingdom. Assessors analysed these and attributed cause to surgical disease, intercurrent disease, the delivery of surgery or anaesthesia, or a combination of those. The study of malpractice closed claims, reported by Dr F.W. Cheney, examined records of 17 insurance companies. Here, only anaesthesia-related claims were reviewed and the reviewers assessed appropriateness of care, involvement of error, and preventability. There is no denominator of the total number of operations represented, so no incidence can be calculated. The outcomes include not only death but other injuries (excluding dental). Dr J.B. Forrest described how the randomised trial among 10 hospitals recorded outcomes in 17 201 patients who were randomised across four anaesthetic regimens (halothane, enflurane, isoflurane and balanced). Nearly 86% of patients had some form of 'outcome' as defined by this study. The vast majority of these, of course, resulted in no untoward long term sequelae. The study represents the kind of methodology that is required to test hypotheses, in this case, 'Do differences exist among the different anaesthetic drugs?'

Dr M.M. Cohen described the Manitoba Study in which adverse outcomes were recorded for approximately 112 000 patients in one large teaching hospital. Here, all patients were carefully screened by a smaller group of anaesthetists, assuring better validity of the data. The overall rate of outcomes is substantially different from that in the randomised trial, because the definitions of 'outcomes' are different. This demonstrates how careful one must be in interpreting and comparing studies.

The study on 'recovery-room-impact-events', described by Dr J.B. Cooper, illustrates yet another outcome measure, similar to that defined in the Manitoba Study. Potentially harmful, anaesthesia-related events, which required intervention and continuing care in the recovery room were recorded. The overall rate of these was not too dissimilar from that in the Manitoba Study. This study illustrated how such outcome measures can be used to test the effects of clinical interventions. But, as Dr Cohen described in her presentation, none is as powerful or as elegant as the randomised trial technique.

Each presentation offered insight into the realities of anaesthetic risk, interpretation of research or news about new activities.

### The Confidential Enquiry into Perioperative Deaths

CEPOD demonstrated that cooperation between anaesthetists and surgeons in outcome studies is possible. The study provides some comfort in revealing that very few people die solely as a result of causes attributable to anaesthesia (1/185 000). Concern still exists over the 14% of patients to whose deaths anaesthesia at least partly contributed. A positive effect of the study was that surgeons and anaesthetists are now meeting to discuss jointly their practices and that reporting of deaths is now established. The identification of inadequate supervision of junior anaesthetists as a frequent mortality-related finding has prompted closer examination of this issue. Dr Lunn explained that the anonymity, confidentiality and legal protection provided were at least partially responsible for the success of CEPOD. He also noted that intense personal contact with participants and their hospitals is required to obtain cooperation.

### Randomised trial of four anaesthetics

Dr J.B. Forrest indicated how difficult it is to organise a massive randomised trial. A particular problem is obtain-

Accepted 9 November 1988.

0003–2409/89/050441 + 03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

is rare and even where it exists, its useful life is short due to ing consensus among a large pool of investigators (22 in this case). Intense attention to detail is required to assure that the participants and their institutions understand the study and adhere to the protocol. Verification of data similarly requires a tremendous commitment of resources. Dr Forrest reported his assessment that, while some differences among the four anaesthetic regimens were identified, these were relatively minor and probably do not contribute in a significant way to anaesthetic risk. He believes that the condition of the patient and the person administering the anaesthetic are probably more important than the drugs.

### *New from Australia*

Dr R. Webb described the foundation of a new Australian Anaesthesia Patient Safety Foundation. It is nonprofit-making and has private financial support. An anaesthesia-incident monitoring study has also been established in Australia and is planned to include 50 hospitals and 500 anaesthetists. Its purpose is to collect critical incidents and analyse that information to share among the Australian anaesthesia community. A vital link in the study will be the person-on-the-spot (POS) located in each participating institution, responsible for motivating cooperation and ensuring credibility of data.

### *Closed claims study*

In describing the closed-claims study, Dr F.W. Cheney reported that analysis of between assessor reliability is an important new component of their work. Such assessments are vital in the design of outcome investigations where reviewers are used. It was comforting to find that among 42 raters of 48 case summaries, there was a high degree of agreement on the appropriateness of care and on the involvement of human error. Agreement on assessing prevention by better monitoring was somewhat less but still quite reasonable. (Specific data will be reported in a manuscript in preparation.) The value of the closed-claims review methodology is demonstrated in the way that it identified an interesting subset of deaths and injuries that followed sudden cardiac arrest from spinal anaesthesia, and in providing information to assess the potential of monitoring technologies to prevent untoward outcomes.[5]

### *The Manitoba study*

The Manitoba study offers many lessons. Careful study design and attention to detail are required for credibility. All the centres must use similar instruments. Code books must be prepared to define all data items; all participants and data coders must be trained and indoctrinated into the objectives of the study. An appropriately designed anaesthesia record can be an instrument for the collection of outcome data. The design of that record must recognise potential difficulties of recording complications. The document for anaesthesia billing may be combined with collection of outcome data and this is a good device for improving compliance. The importance of a dedicated, well trained coordinator, with appropriate clinical background and the respect of other clinicians is vital to the success of such efforts.

### *Recovery-Room-Impact Events* (RRIE)

Dr J.B. Cooper in describing the study of RRIEs, noted how carefully planned experimental designs can be altered by uncontrollable events. A 6-month control period and a 6-month experimental period were planned to test for the effects of feedback of information to participants. This was based on estimates of the required sample size for sufficient statistical power to test the hypothesis. Plans to introduce pulse oximetry sooner than had otherwise been anticipated forced a change in the sampling periods. The smaller sample size impeded testing of the hypothesis although reasonable statistical power was still obtained. This illustrates the extreme difficulty in controlling all of the potentially confounding variables in longitudinal clinical experiments.

### *Other studies*

Studies in Norway (Dr S.E. Gisvold), and in Demark (Drs T. Pederson and T. Moeller) were mentioned briefly. Dr A. Bunatian briefly reported on data collected recently in Moscow. Dr G.G. Harrison summarised results of studies in South Africa that reflect the decreasing incidence of deaths attributable to anaesthesia over the past several decades (0.4/1000 to 0.07/1000).

### *Fatigue survey*

Dr J.S. Gravenstein described the Anaesthesia Patient Safety Foundation (USA) survey of fatigue among anaesthesiologists. His report prompted interest from two other countries in which it is hoped that the same survey will be distributed. The discussion following his presentation indicates that fatigue and work hours are of interest in other countries. In Brazil, the maximum number of working hours for house staff is limited to 60 hours by law. Dr J. Zelcer reported a study in Australia to assess the effects of fatigue on performance. It is noted that regulations which limit the duration of continuous work exist in various states of Australia and Canada.

### *Monitoring in Europe*

Dr H. Schwilden presented results of a survey recently conducted in several European countries set up to assess what anaesthetists monitor during anaesthesia. His presentation emphasised that there are wide variations in anaesthesia practices among European states. A large majority of respondents said that they had experienced a situation where a monitoring device detected a life-threatening complication before they would have themselves, based on clinical signs alone. There is apparently a need for education among anaesthesiologists about the function of various forms of monitoring. The implication is that efforts are needed in training programmes since the majority of the sampled anaesthesiologists were residents.

### *Personality*

Dr J.M. Davies reviewed the literature on the personality of anaesthetists and the relationship between this and accidents and the process of selection of trainees. Studies have evaluated anaesthetists' personalities, but it is not clear if the specialty constitutes a distinct 'species'. No profile of an accident-prone anaesthetist is known. A 4-year, prospective study of residents in Canada, Eire, and France is planned to establish the personality characteristics and attitudes of anaesthesia practitioners.

### *Safety in developing countries*

Dr Z. Vieira spoke about patient safety in Latin America, where facilities for anaesthesia are very different from the industrialised countries. Electronic monitoring equipment

## The control of post-thoracotomy pain

The valuable paper by Gough *et al* (*Anaesthesia* 1988; **43:** 730–3) outlines their routine for performing midthoracic epidural punctures and cannulation under general anaesthesia. Unhappily, the authors go on to encourage others to follow their practice, with the reassurance that we should not worry about spinal cord injury from thoracic epidurals under general anaesthesia since 'the evidence at the moment is that damage does not occur'. This astonishing statement is accompanied by two references. One relates to a numerically impressive series of 26 127 single-shot obstetric epidurals carried out in awake patients, and presumably below the termination of the cord,[1] and therefore irrelevant to the issue at stake. The second reference cites 58 thoracic epidural cannulations performed under general anaesthesia; a dural tap arose in one of these and the epidural space could not be identified in two others: that is a near-miss rate of 2% in round numbers and a technical failure rate of 5%.[2] These citations are scarcely evidence and it would be a major tragedy if others less skilled than Dr Gough and his colleagues were tempted to risk their luck and their patients' spinal cords by performing thoracic epidurals as a routine measure in unconscious patients.

There *is* documentation that damage to the spinal cord can occur and has occurred,[3–5] and confidential medico-legal files suggest that the incidence of harm from this practice is higher than reported. Commonsense and elementary anatomy tell us that damage will continue to occur in the future if the cardinal sign of lancinating pain from cord puncture is obscured by general anaesthesia, and in my view this risk should only be undertaken in exceptional circumstances.

What are the odds that all will be well, and that since nothing appears to have gone wrong so far everything will be all right? To achieve a 99.9% probability that all will continue to be well in a blameless series of *n* cases, *n* becomes the denominator of a ratio where the zero numerator is replaced by the number 6.9.[6] Thus, having achieved a successful series of 1000 cases, the 99.9% probability that the next patient will be all right would command betting odds of 145:1. Not bad if one is betting on a horse and is prepared to put down big money to win a little—but one's own spinal cord?

Let me carry this matter a step further to a personal level where one puts oneself next on the list. How many of Dr Gough's team, or the readership of *Anaesthesia* would be ready to submit to thoracic epidural cannulation, let us say for an important experiment, or even a thoracotomy if unfortunate enough to need chest surgery, awake or under general anaesthesia? Many of us with any degree of professional curiosity would be willing to accept the first offer, awake. But would we be so foolhardy as to accept the second option of being asleep, unless driven to it by extraordinary circumstances?

My own practice has been to submit myself as a subject to epidural punctures when necessary, but always awake and unpremedicated, as are my patients, and to restrict thoracic puncture in unconscious patients to the gravest indications, such as status asthmaticus or complicated postoperative situations where the surgical team perceives some unique advantage and where other avenues seem to offer a lower benefit:risk ratio.

We should not delude ourselves. Regional anaesthesia has much to offer but in the words of Green 'it is less forgiving then general anaesthesia of anything less than perfection'.[7] When fatal accidents happen under general anaesthesia we bury the dead. Survivors from major neurological complications of regional anaesthesia live on in bitterness and as a reproach to our shortcomings and to the techniques we have used or abused. Blind invasion of the spinal canal, even in the most skilled hands, can never be as safe asleep as awake. Why risk the added risk?

*Medical Center of Delaware,*
*4755 Ogletown-Stanton Road,*
*Newark, Delaware 19718,*
*USA*

P.R. Bromage

### *References*

1. Hellmann K. Epidural anaesthesia in obstetrics: a second look at 26127 cases. *Canadian Anaesthetists' Society Journal* 1965; **12:** 398–404.
2. Conacher ID, Paes ML, Jacobson L, Phillips PD, Heaviside DW. Epidural analgesia following thoracic surgery. A review of two years' experience. *Anaesthesia* 1983; **38:** 546–51.
3. Bonica JJ, Backup PH, Anderson CE, Hadfield D, Crepps WF, Monk BF. Peridural block: analysis of 3 637 cases and a review. *Anesthesiology* 1957; **18:** 723–84.
4. Bromage PR. *Epidural analgesia.* Philadelphia: W.B. Saunders, 1978: 667.
5. Honkomp J. Zur Begutachtung bleibender neurologischer Schaden nach Periduralanaesthesie. *Der Anaesthesist* 1966; **15:** 246–8. Judging permanent neurological damage after peridural anesthesia. (English title).
6. Hanley JA, Lippman-Hand A. If nothing goes wrong, is everything all right? Interpreting zero numerators. *Journal of the American Medical Association* 1983; **249:** 1743–5.
7. Greene NM. Labat Lecture. Challenges and opportunities: the future in regional anesthesia. *Regional Anesthesia* 1987; **12:** 113–21.

### *A reply*

Thank you for allowing us to reply to Dr Bromage's letter in which he makes a number of valid points.

However, our article was not intended as an encouragement for all and sundry to start catheterising the thoracic epidural spaces of anaesthetised subjects without any thought of the possible risks and consequences of spinal cord damage. We have described a technique with which we have had considerable experience and which we consider to be safe in our hands. A recent reference states that 'the occurrence of permanent neurological sequelae is so rare that there is no quotable figure of incidence'.[1]

The advent of epidural techniques for analgesia during labour has meant that most anaesthetists are well practised in the technique of placing epidural catheters. By the time our junior anaesthetists come to perform a thoracic epidural, they have done scores if not hundreds of epidurals on labour wards. Further, in Cardiff, the inexperienced anaesthetist is not allowed to insert a thoracic epidural into an anaesthetised patient. Moreover, initial experience with thoracic epidurals is usually gained in awake patients with multiple rib fractures. Only when we were satisfied with the safety of the technique did we start to use it in anaesthetised patients. A census of local colleagues indicates that most perform thoracic epidurals under general anaesthesia. Benumof, in a review of the management of postoperative pain, states that epidurals can be inserted either before anaesthesia or before emergence from anaesthesia.[2]

We agree that the evidence to support the safety of our technique is scant, but so is the evidence against. Unpublished data from Cardiff include more than 1000 cases with no recorded incidence of spinal cord damage and a less than 1% incidence of dural tap; the latter is far less a near-miss than in the upper lumbar and lower thoracic epidural space because of the angulation of the Tuohy needle. Our failure rate of about 10% reflects, in our opinion, strict adherence to a 'Do-No-Harm' policy: we accept failure early rather than persevere.

Finally, because of the restriction of limited bed-availability and operating time, the majority of our thoracic patients have a bronchoscopy by the surgeon immediately before surgery. Occasionally the lesion is found to be inoperable. These patients would have had a thoracic epidural inserted unnecessarily if this were to be done before anaesthesia. We do not find this to be acceptable practice.

Theoretically Dr Bromage may be right. In practice, however, we believe that in our hands our technique is safe and has very considerable benefits for the patient who is undergoing thoracic surgery. We also believe that our observations confirm our belief. We leave it to our colleagues to make their own decisions.

*University Hospital of Wales,*
*Cardiff CF4 4XW*

R.S. Vaughan
J.D. Gough

*References*

1. Conacher ID. Pain relief following thoracic surgery. In: Gothard JWW, ed. *Clinical anaesthesiology. Thoracic Anaesthesia,* March 1987. London: Baillière Tindall.
2. Benumof JL. Management of postoperative pain. In: *Anaesthesia for thoracic surgery.* Philadelphia: W.B. Saunders, 1987.

## Anxiety and informed consent

Dr Antrobus (*Anaesthesia* 1988; **43:** 267–9) measured anxiety levels in 43 female patients using two procedures in a recent study of the influence of anxiety in affecting a patient's decision to consent to be included in a medical study. The first was the stait-trait anxiety inventory[1] (STAI) which consists of 20 questions and gives a score between 20 for low-anxiety and 80 for a high-anxiety level. The second procedure was to use a 10-cm linear analogue scale[2] (LA) in which the left-hand end was identified to patients by the phrase, 'I do not feel anxious at all' and the right-hand end by the phrase, 'I could not feel more anxious'. A patient's anxiety score was measured by the distance in millimetres from the left-hand end of the scale to the position indicated by the patient.

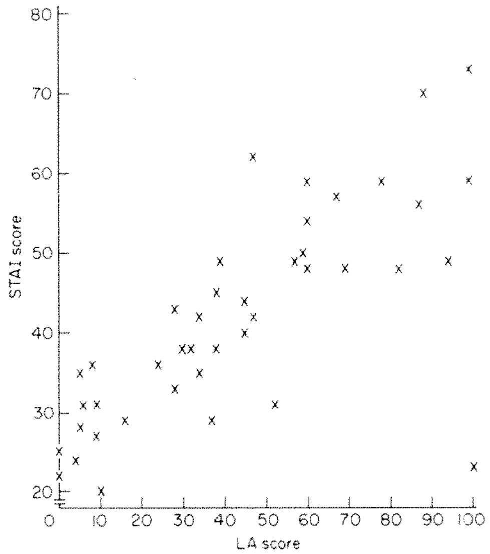


**Fig. 1.** Plot of STAI score against LA score.

A scatter-plot of the LA scores against the STAI scores for the 43 patients reveals, apart from a single individual, an approximately linear relationship. The Spearman correlation coefficient for these data has a large positive value $r = 0.75$ which is significant at the 0.01% level.

The single outlying individual can be explained as a patient with a low anxiety level as assessed on the STAI scale and who has grossly exaggerated her own anxiety on the LA scale. The best-fitting straight line to the data with this individual excluded from the data is given by:

STAI score = 26.3 + 0.382 × (LA score).

Hence when given a patient's LA score one can use the straight line relationship to assess the approximate STAI anxiety level for the patient quickly. For example, for a LA score of 50 an individual's predicted STAI level is 45.4 (95% confidence limits 13.9) while for a LA score of 10 the STAI is 30.1 (95% confidence limit 14.1). One difference between the results for the two measures is that while patients readily assign anxiety LA scores anywhere in the range 0 to 100 the STAI method restricts values to the interval 20 to 80.

In practice, using the linear analogue scale is quick, cheap, and simple to administer. It gives a rough guide to a patient's anxiety level. Whether patients will believe those who administer it is another matter because analogues seem so 'simple'.

*University of Leeds,*
*Leeds LS2 9JT*

A.J. Baczkowski

*References*

1. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. *Manual for the Stait-Trait Anxiety Inventory; STAI (Form Y).* Palo Alto, CA: Consulting Psychologists' Press, 1983.
2. Aitken RCB. Measurement of feelings using visual analogue scales. *Proceedings of the Royal Society of Medicine* 1969; **62:** 989–93.

## Re-expansion pulmonary oedema

We found the case report by Khoo and Chen (*Anaesthesia* 1988; **43:** 486–9) very interesting. This is a report of an unusual case of re-expansion pulmonary oedema (RPE), which sheds new light on the points made in the above article.

A 65-year-old retired miner with chronic dyspepsia was investigated for haematemesis. Adenocarcinoma of the midoesophagus was diagnosed after endoscopy. An Ivor Lewis two-stage oesophagectomy was planned.

The procedure lasted for 4 hours 40 minutes during which time the patient received crystalloid 1000 ml and colloid 1500 ml. Blood loss was not excessive and all intra-operative variables (pulse, blood pressure, oxygen saturation) remained stable. The right lung was deflated for 2 hours during the thoracic stage of the resection, and before closure of the chest this lung was forcefully re-expanded with manual positive-pressure ventilation. The patient became restless, sweaty, with a tachycardia and was peripherally cool immediately after reversal and extubation. His chest radiograph showed unilateral right-sided pulmonary oedema and arterial blood gas analysis revealed hypoxic respiratory acidosis. The diagnosis of re-expansion pulmonary oedema was made and treatment instigated with frusemide 40 mg intravenously and 100% oxygen via a facemask. His condition rapidly improved within an hour and radiographic appearances had resolved within 8 hours.

Khoo and Chen highlighted the factors associated with the development of RPE: the duration and severity of collapse and the speed of re-expansion. RPE is thought to be due to increased pulmonary capillary permeability.[1] Prolonged collapse may cause anoxic damage to the capillaries,[2] rapid re-expansion may cause mechanical damage by overdilating the capillaries.[3]

This case illustrates that rate of re-expansion may be more important than duration of collapse in the development of RPE. This view was shared by Mahfood *et al.* who reported 15 cases where RPE occurred after short-term pulmonary collapse due to pneumothorax.[3]

RPE is commonly described after treatment of lung collapse secondary to pneumothorax or pleural effusion.[3] However, RPE has not been commonly documented after manual positive-pressure reinflation before closure of thoracotomy. The incidence of RPE in this situation may be underestimated as aspiration pneumonia, or atelectasis may be more commonly diagnosed. We feel that RPE should be considered whenever respiratory distress develops after an operation in which a collapsed lung has been forcefully re-expanded. One should be aware of RPE and that it is readily treated but potentially fatal.

*Killingbeck Hospital,*
*Leeds LS14 6VQ*
D.A. Waller
N. Turner

*References*

1. Sprung CL, Loewenherz JW, Baier H, Hauser MJ. Evidence for increased permeability in reexpansion pulmonary edema. *American Journal of Medicine* 1981; **71**: 497–500.
2. Pavlin DJ. Lung reexpansion—for better or worse? *Chest* 1986; **89**: 2–3.
3. Mahfood S, Hix WR, Aaron BL, Blaes P, Watson DC. Reexpansion pulmonary edema. *Annals of Thoracic Surgery* 1988; **45**: 340–5.

---

## Retained nasopharyngeal airway

A 39-year-old 60 kg mentally subnormal male patient in a residential care hospital suffered a chronic one-sided nasal discharge for over a year. He had several medical examinations for this and was prescribed ointment. He was eventually referred to an ENT surgeon for examination under anaesthetic to exclude a foreign body. Anaesthesia was impossible when first scheduled because he refused an injected premedication and refused to leave the ward for the trip to the operating theatre.

He was heavily sedated at the second attempt with lorazepam 4 mg 6 hours and temazepam 30 mg 90 minutes before operation. He was eventually brought with some difficulty to the anaesthetic room and was swiftly induced with methohexitone and suxamethonium to allow laryngoscopy for intubation. On inspection, 3 cm of pale blue plastic nasopharyngeal airway were seen projecting into his pharynx from behind the soft palate. A complete Portex 6 mm nasopharyngeal airway was removed through the mouth by the anaesthetist, with some minor bleeding and without the need to proceed to intubation.

This patient had received dental treatment under general anaesthetic 1 year and 2 months beforehand. Presumably this airway slipped into the nasal cavity during the recovery period and remained there since.

One can only note the minimal flange on Portex nasopharyngeal airways in relation to their cross-sectional diameter compared with the generous flange on Bardex or Wood–Smith airways, and draw attention to this as a potential hazard with this airway.

*Wexham Park Hospital,*
*Slough, SL2 4HL Berks*
B.L. Smith

*A reply*

The Portex Nasopharyngeal Airway is manufactured from materials which attempt to reconcile the somewhat conflicting aims of ease of intubation and kink-resistance, and of protection of delicate tissues. The necessary (and, we believe, successful) compromise achieved in the material formulation does, however, produce one technical limitation, *viz* the amount of 'belling' that can be obtained to produce the flange. This is normally more than adequate in the case of the larger sizes, but it must be acknowledged that the flange on the smallest (6 mm ID) airway, as used in the present case, is under certain clinical conditions small enough to allow entry of the airway into the nasal cavity and beyond.

Portex, for this reason and after a similar incident some 2 years ago, issued a general advisory notice to users, to warn of this possible risk. It was suggested then, and continues to be our recommendation: that the use (and subsequent removal) of a nasopharyngeal airway be specifically recorded on the patient's records/notes; and that in case of doubt, adequate safety precautions be taken to prevent movement.

The less-than-hi-tech solution proposed to achieve the latter was to pass a safety-pin at right-angles through the distal end of the airway. Like so many simple solutions, this has found favour with many users and a suitable safety-pin is now supplied in the pack of all airways, so that the option of the 'enlarged' flange can be taken with minimum inconvenience. In the meantime, of course, the design of the product is under constant review, and clinical trials using materials that allow the formation of a larger flange are being carried out. Our concern remains that the features of ease-of-intubation, kink-resistance and the minimalisation of tissue-damage should not in any way be compromised.

*Portex Ltd,*
*Hythe,*
*Kent*
A.P. Mobbs

## Laparoscopy and vagal arrest

We report a case of cardiac arrest during laparoscopy which we believe to be vagally mediated.

A healthy 39-year-old woman was admitted to hospital for laparoscopic sterilisation. Pre-operative assessment was unremarkable. The usual anaesthetic monitors, including capnograph and pulse oximeter, were employed. Anaesthetic technique included tubocurarine 3 mg and fentanyl 50 $\mu$g before induction with sodium thiopentone 275 mg and suxamethonium 120 mg. Later, vecuronium 3 mg was given for continued neuromuscular blockade. Normocapnia was maintained. The Verres' needle was introduced at the lower margin of the umbilicus with the patient in the lithotomy position. The patient developed a rapidly progressive sinus bradycardia, which ended in asystole and was accompanied by a flat tracing on the pulse oximeter after 500 ml $CO_2$ were insufflated. Atropine 0.6 mg was immediately given and the surgeon was asked to withdraw the Verres' needle. Sinus rhythm resumed after about 15 to 20 seconds of asystole, and shortly thereafter a tachycardia ensued. The procedure was cancelled at the surgeon's request, and the patient recovered without incident.

Several authors[1,2] have noted a high incidence of arrhythmias in patients who have laparoscopy, but reports of bradycardia leading to sinus arrest are rare. Carmichael[3] noted three cases of bradycardia during $CO_2$ insufflation, one of which led to an unobtainable pulse, and attributed it to reflex vagal stimulation from peritoneal distension. However, because there was no mention of electrocardiographic monitoring in the report, the exact cardiac rhythm is unclear.

Vecuronium is associated with bradycardia and sinus arrest in several reports[4–7] and also with both complete atrioventricular block[8] and with sinus node exit block.[9] However, we believe this to be the first reported case of sinus arrest during a laparoscopic procedure in which vecuronium was used. Cozanitis *et al.*[10] suggested that glycopyrronium protected against undesirable vagal activity when vecuronium was used. The bradyarrhythmias (including this case) are likely attributable to increased vagal tone which occurs reflexly from traction on the peritoneum. This effect is often masked by vagolytic or sympathomimetic effects of drugs such as pancuronium. However, if drugs free from cardiovascular effects such as vecuronium are used this reflex response is not masked unless an anticholinergic is also administered. Consequently, it may be advisable to use an anticholinergic concomitantly with non-vagolytic muscle relaxants such as vecuronium to avoid this type of incident.

*Toronto General Hospital,*
*Toronto,*
*Canada MJ9 2C4*

D.J. Doyle
P.W.S. Mark

### *References*

1. Scott DB, Julian DG. Observations on cardiac arrythmias during laparoscopy. *British Medical Journal* 1972; **1:** 411–3.
2. Harris MNE, Plantevin OM, Crowther A. Cardiac arrhythmias during anaesthesia for laparoscopy. *British Journal of Anaesthesia* 1984; **56:** 1213–7.
3. Carmichael DE. Laparoscopy—cardiac considerations. *Fertility and Sterility* 1971; **22:** 69–70.
4. Kirkwood I, Duckworth RA. An unusual case of sinus arrest. *British Journal of Anaesthesia* 1983; **55:** 1273.
5. Milligan KR, Beers HT. Vecuronium-associated cardiac arrest. *Anaesthesia* 1985; **40:** 385.
6. May JR. Vecuronium and bradycardia. *Anaesthesia* 1985; **40:** 710.
7. Higgins M, Thorp JM. Non vagolytic anaesthetic sequence—sinus arrest. *Anaesthesia* 1986; **41:** 89–90.
8. Williams HD, Studd C. Vecuronium bromide and complete atrioventricular block. *Anaesthesia* 1985; **40:** 205.
9. Yeaton P, Teba L. Sinus node exit block following administration of vecuronium. *Anesthesiology* 1988; **68:** 177–8.
10. Cozanitis DA, Pouttu J, Rosenberg PH. Bradycardia associated with the use of vecuronium. A comparative study with pancuronium with and without glycopyrronium. *Anaesthesia* 1987; **42:** 192–4.

---

## Complete heart block following glycopyrronium/neostigmine mixture

Glycopyrronium is used increasingly to antagonise the muscarinic effects of neostigmine during the reversal of neuromuscular blockade. We report a case of complete heart block following the administration of a mixture of glycopyrronium and neostigmine.

The patient was an obese, 45-year-old woman who presented for mastectomy and axillary clearance. She was a type II diabetic controlled on glibenclamide and suffered from hypertension, for which she received atenolol 100 mg once daily. She described herself as allergic to opiates, which we therefore decided to avoid if possible. She was premedicated with temazepam 20 mg, anaesthesia was induced with thiopentone 250 mg and tracheal intubation facilitated with suxamethonium 100 mg. The patient's lungs were ventilated, after administration of vecuronium 7 mg, with 66% nitrous oxide in oxygen and enflurane 1%. Diclofenac 75 mg was given by intramuscular injection before the procedure started.

The surgery, which lasted for 2 hours, proceeded uneventfully. Blood loss was minimal and systolic blood pressure remained stable throughout at 120–140 mmHg with a pulse rate of 60–70 beats/minute and sinus rhythm. Two increments of vecuronium 1 mg were required.

The volatile agent was discontinued at the end and a mixture of glycopyrronium 0.5 mg with neostigmine 2.5 mg was administered for reversal of neuromuscular blockade. The heart rate changed about a minute later from sinus rhythm at a rate of 74 beats/minute to complete heart block with a ventricular rate of 35 beats/minute. Atropine 0.6 mg was injected intravenously and the ECG recording reverted rapidly to sinus rhythm at a rate of 90 beats/minute. Recovery was thereafter uneventful.

Discussion with colleagues revealed a similar case where complete heart block occurred on administration of neostigmine and glycopyrronium after thyroidectomy, in a patient who was treated with the beta blocker nadolol before surgery.

Unopposed, the muscarinic action of neostigmine on the heart causes bradycardia, A-V conduction defects and even cardiac arrest. Atropine has until recently been the drug of choice to antagonise these muscarinic effects but it has both a shorter onset time and shorter duration of action than neostigmine. This leads to an initial tachycardia with a subsequent risk of bradycardia once the effect of the atropine has worn off. Glycopyrronium and neostigmine have a similar onset and duration of action leading to a more stable heart rate.[1] It has been shown that a dose of glycopyrronium 10 $\mu$g/kg provides the most stable heart rate when given in a mixture with neostigmine 50 $\mu$g/kg; a ratio of 0.2 mg glycopyrronium for every mg of neostigmine. This was the dose ratio we used, a low dose of each drug when calculated on a μg/kg basis. The same study showed that a lower dose of glycopyrronium, 5 μg/kg, gave an unacceptably high incidence of conduction disturbances.[2] In patients on beta blockers where A-V conduction velocity is already slowed,[3] cholinergic stimulation of muscarinic receptors may act in a synergistic fashion, making A-V conduction defects more likely. It may be that these patients should receive a higher dose of glycopyrronium to guard against this effect.

*Ninewells Hospital,*
*Dundee DD1 9SY*

M. LONSDALE
J. STUART

*References*

1. MIRAKHUR RK, DUNDEE JW. Glycopyrrolate: pharmacology and clinical use. *Anaesthesia* 1983; **38:** 1195–1204.
2. MIRAKHUR RK, DUNDEE JW, JONES CJ, COPPEL DL, CLARKE RSJ. Reversal of neuromuscular blockade: dose determination studies with atropine and glycopyrrolate given before or in a mixture with neostigmine. *Anesthesia and Analgesia* 1981; **60:** 557–62.
3. FRISHMAN W, SILVERMAN R. Clinical pharmacology of the new beta-adrenergic blocking drugs. Part 2. Physiologic and metabolic effects. *American Heart Journal* 1979; **97:** 797–807.

## A reaction to midazolam: a topical solution

A 75-year-old gentleman who weighed 77 kg and classified ASA 1 was anaesthetised for a left total hip replacement. His other recorded anaesthetic was for a cystoscopy performed under nitrous oxide and oxygen after a propofol, fentanyl and midazolam induction during which there were no problems noted. He was given morphine 5 mg intramuscularly as premedication on this occasion and on arrival in the anaesthetic room an intravenous infusion of compound sodium lactate solution was commenced as a preload. A spinal anaesthetic was performed at $L_{3-4}$, 0.5% plain bupivacaine 3.5 ml was given via a 25-G spinal needle. He was given cefuroxime 750 mg at the beginning of the procedure, and then the crystalloid was replaced with polygeline (Haemaccel). Shortly after this he was given midazolam as sedation: he then became agitated, having developed an intense pruritus which involved the head, neck and trunk. Much to the consternation of ourselves and the surgeons, he began to scratch the affected areas, so was given chlorpheniramine 10 mg, intravenously followed by further increments of midazolam, which calmed him down.

Polygeline was suspected to be the causal agent, and was replaced with crystalloid; there was no cardiovascular or respiratory instability. He progressed well postoperatively and his pruritus resolved after several hours. His presumed allergy to polygeline was noted and no further action was taken.

Three weeks later the patient underwent right total hip replacement. The same anaesthetic technique was used as before after premedication with temazepam 20 mg, but polygeline was not used. He again required sedation, and midazolam 2 mg was administered. He again complained of intense pruritus within 5 minutes with no cardiovascular or respiratory problems. Intravenous chlorpheniramine made little difference, and so a tube of Caladryl cream was obtained from the pharmacy. This produced good symptomatic relief, as well as much eyebrow raising and comments from our surgical colleagues concerning our 'Hands on' technique!

Midazolam was implicated as the drug responsible for the pruritus in the absence of any other possible causal factor. A report about this allergic reaction was made to The Committee on Safety of Medicines and to Roche Products Ltd. The manufacturers have stated that they know of one other similar episode reported to them, but that no further details are available.

*Royal Naval Hospital,*
*Gosport,*
*Hants, PO12 2AA*

A. YATES
D. RUSSELL

## Airway obstruction in epidermolysis bullosa

Epidermolysis bullosa is a skin disease characterised by the formation of bullae in response to minimal trauma. The lesions are prone to rupture leaving a bleeding exudative surface which may heal with severe scarring. Anaesthetists need to be aware of this condition, despite its rarity, because the involvement of the mucous membranes theoretically contraindicates laryngoscopy and tracheal intubation. The production of bullae in the airway could result in potentially fatal obstruction, although this does not appear to have been reported. We were recently asked to anaesthetise a 3-month-old baby with airway obstruction secondary to a bulla which apparently had formed spontaneously.

The patient was delivered by Caesarean section, and, at birth, the fingers were noted to have a drum-stick appearance with multiple skin erosions. Further 'friction burns' on the elbows and buttocks prompted a dermatological referral. Skin biopsy confirmed the diagnosis of epidermolysis bullosa lethalis. She was referred to this hospital with a history of loss of voice, cough, and stridor becoming progressively worse over 4 days. She had severe respiratory distress, with little air entry and obvious cyanosis by the time a decision had been made to transfer her to the operating theatre for direct laryngoscopy and possible tracheostomy.

Monitoring was established with a pulse oximeter and an electrocardiograph using the least adhesive electrodes available. No attempt was made to set up an intravenous infusion with the baby awake; there was intense vasoconstriction and any struggling accentuated the airway obstruction. Anaesthesia was induced with halothane in oxygen via a soft facemask, preserving spontaneous ventilation. A large, fibrosing bulla was seen lying just above the vocal cords at laryngoscopy. Maintenance of anaesthesia and oxygenation was attempted by directing a flow of gas into the mouth during surgery, but there were episodes of desaturation which necessitated alternating surgical and anaesthetic access to the airway. The lesion was successfully removed despite these difficulties, without recourse to tracheal intubation or tracheostomy. The stridor was relieved immediately and no complications were observed overnight in the high dependency area. The infant was discharged 4 days later.

We believe this was an unusual anaesthetic problem, and would be interested in others!

*The Children's Hospital,*
*Ladywood,*
*Birmingham*

G.C. FISHER
D.A.A. RAY

## Postoperative pain after laparoscopic sterilisation

The study by Davis and Millar (*Anaesthesia* 1988; **43:** 796–7) verifies clinical impressions that laparoscopic sterilisation is a more painful procedure than diagnostic laparoscopy. We approached this problem by applying 1% etidocaine topically to the fallopian tubes from uterus to fimbriae prior to tubal banding.[1] Others have used bupivacaine with some success.[2]

We have data which compare 1% etidocaine 2 mg/kg with 0.75% bupivacaine 1.5 mg/kg. Significantly less pain was reported in those patients who received etidocaine (Table 1). Etidocaine differs significantly from bupivacaine in fat solubility and pKa.

In 22 patients we have established the safety of these doses for patients who receive general anaesthesia. The mean peak concentrations were 501.8 ng/ml for etidocaine and 468 μg/ml for bupivacaine. Both doses resulted in blood concentrations of one quarter of the reported minimal convulsive level of 2 μg/ml in monkeys and one eighth of the arterial convulsive level in humans.

All laparoscopic sterilisations have received topical etidocaine prior to tubal occlusion since 1983. We have documented a marked reduction in postoperative opioid use and fewer admissions to the hospital overnight.

*Magee-Women's Hospital*
*Pittsburgh, Pennsylvania 15213*
*USA*

R. McKenzie

*References*

1. McKenzie R, Phitayakorn P, Uy NTL, Tantisira B, Wadhwa RK, Vicinie AF. Topical etidocaine during laparoscopic tubal occlusion for postoperative pain relief. *Obstetrics and Gynecology* 1986; **67:** 447–9.
2. Spielman FJ, Hulka JF, Ostheimer GW, Mueller RA. Pharmacokinetics and pharmacodynamics of local analgesia for laparoscopic tubal ligations. *American Journal of Obstetrics and Gynecology* 1983; **146:** 821–3.

**Table 1.** Abdominal pain reported after topical application of etidocaine and bupivacaine during tubal occlusion.

| | | Degree of pain | | | | |
|---|---|---|---|---|---|---|
| Group | *n* | Nil* | Mild | Moderate* | Severe | Number of observations |
| Etidocaine | 11 | 28 | 13 | 1 | 0 | 42 |
| Bupivacaine | 11 | 13 | 17 | 12 | 0 | 42 |

* $p < 0.05$
† Four observations could not be obtained: in group E, one on arrival at recovery room and one at 2 hours; in group B, two on arrival at recovery room.

## Cuff dilatation of a tracheostomy track

A tracheostomy can close very rapidly when the tube is removed. This can be a problem, as illustrated by the following report.

A middle-aged man was discharged to the ward from the Intensive Care Unit, after recovery from postoperative acute respiratory and renal failure. A few days later his 9.0-mm cuffed tracheostomy tube (Portex Ltd) was removed and the stoma covered with a waterproof dressing. The next day the patient developed acute pulmonary oedema complicated by sputum retention. Reinsertion of the tracheostomy tube was requested so that tracheal toilet and controlled ventilation of the lungs could be achieved.

The stoma had almost completely closed, but I was able to pass an introducer from a Mini-Trach kit (Portex Ltd) gently along the narrow track into the trachea. A 4.0-cm Mini-Trach tube was inserted over the introducer fairly easily. The ENT surgeons were consulted and suggested that a Bowlby tracheal dilator be used to widen the track. This was tried but with little effect; however I was able to pass a 5.0-mm cuffed disposable tracheal tube (Portex Ltd) through the re-established tracheostomy and dilate the path by intermittent inflation of the cuff during withdrawal of the tube. The most stenosed part of the track could be felt and the cuff was sited at that point. A 6.0-mm cuffed disposable tube was then passed and the process repeated; I then inserted a 7.0-mm cuffed tracheostomy tube with relative ease and secured it in place. This tube was large enough to enable IPPV, which in the event was not necessary. The whole procedure was accomplished with minimal discomfort without sedation, analgesia or local anaesthetic.

The pulmonary oedema resolved with diuretics and the tracheal tube was left in for 5 days while the patient completed a course of antibiotics for his chest infection.

Intermittent cuff inflation during withdrawal of a tracheal tube is suggested as a method of dilating a stenosed tracheostomy.

*Southmead Hospital,*
*Bristol BS10 5NB*

A.P. Madden

## Emergency radiotherapy in a patient with a mediastinal lymphoblastoma

Drs John and Narang (*Anaesthesia* 1988; **43:** 864) report on a 12-year-old boy with an anterior mediastinal mass who developed severe airway obstruction after induction of anaesthesia. This could only be relieved by microlaryngeal tubes inserted into each main bronchus. Chemotherapy was started immediately because the tumour was shown to be a T-cell lymphoma and the trachea extubated on the sixth postoperative day when there was evidence of incipient shrinking of the tumour mass. Radiotherapy is not only an alternative to chemotherapy in pre-operative treatment of such patients, as suggested by the authors, but can also be a very effective emergency treatment, as illustrated by this case report.

A 43-year-old man with a large tumour which extended from the thyroid gland to the pericardium and embraced the ascending aorta and part of the aortic arch was presented for surgery. He complained of exertion dyspnoea and dysphagia; his $Pa\text{O}_2$ was 8.9 kPa, the $Pa\text{CO}_2$ 4.1 kPa on air. An open biopsy was performed under general anaesthesia with thiopentone and suxamethonium for

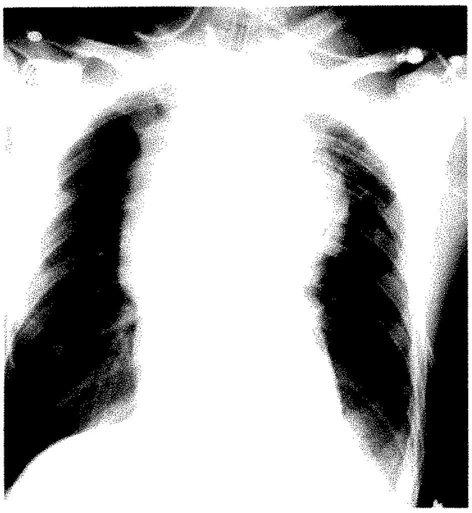


**Fig. 1.** Chest X ray of a 43-year-old patient with t-lymphoblastoma prior to emergency radiotherapy. A large mediastinal mass is present that prevents a venous catheter on the left arm from entering the vena cava superior.

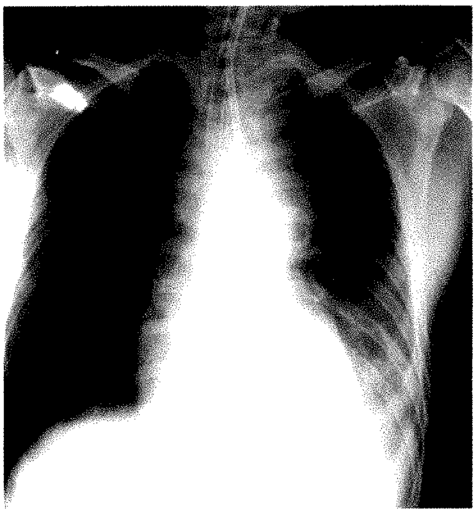


**Fig. 2.** Chest X ray after 4 days of radiotherapy that shows shrinking of the tumor mass. A central venous catheter has now been successfully inserted through the right brachial vein.

induction and halothane and nitrous oxide/oxygen during maintenance. Anaesthesia proceeded uneventfully, with a pulse oximeter reading of 95% ($F\mathrm{IO}_2$ 0.5) apart from moderately high inflation pressures. However, when room air was breathed at the end of the anaesthetic, the saturation decreased to 80%, and it was decided to continue controlled ventilation. An arterial blood sample ($F\mathrm{IO}_2$ 0.50) revealed a $P\mathrm{aO}_2$ of 10.4 kPa and a $P\mathrm{aCO}_2$ of 5.6 kPa. A central venous catheter, easily introduced through the basilic vein could not be advanced into the superior cava vein (Fig. 1). Bronchoscopy showed narrowing of the trachea and both main bronchi whose orifices were barely visible. The tumour was meanwhile classified to be a T-lymphoblastoma so emergency radiotherapy was started on the day of the operation. The patient was exposed to a Co-60 generator and received a radiation dose of 4 × 3 Gy on days 1, 2, 4, and 5. Corticoids, theophylline and fenoterol were also given. The blood gases were satisfactory on days 1 and 2 but deteriorated on day 3 when the left main bronchus was completely obstructed by secretions. Emergency bronchoscopy and extensive bronchial toilet improved oxygenation and the $F\mathrm{IO}_2$ could now gradually be reduced. A central venous line was established on the same day using a peripheral vein. On day 5, concomitant with an impressive reduction in tumour size on the chest X ray (Fig. 2) bronchoscopy revealed that the left and right main bronchus were visible and there was no further narrowing. All sedative drugs were discontinued. The patient's trachea was extubated on his sixth postoperative day and he was transferred to the ward. He had four additional radiations of 2 Gy each. Mackie and Watson, in their otherwise excellent review on the subject[1] mistakenly cite a 13-month-old boy as having emergency radiotherapy[2] but he actually received cytotoxic drug therapy during controlled ventilation. This case report may therefore be the first report of the efficacy of acute radiation therapy in a ventilated patient with a mediastinal tumour and respiratory problems.

*University Hospital,*
*Würzburg,*
*West Germany*

M.J. SOLD
TH. FEYERABEND
G. LAZARUS

## *References*

1. MACKIE AM, WATSON CB. Anaesthesia and mediastinal masses. A case report and review of the literature. *Anaesthesia* 1984; **39:** 899–903.
2. BRAY RJ, FERNANDES FJ. Mediastinal tumour causing airway obstruction in anaesthetised children. *Anaesthesia* 1982; **37:** 571–5.

*Anaesthesia*, 1989, Volume 44, pages 452–453

# Book reviews

**Neural blockade in clinical anaesthesia and management of pain, 2nd edn** 452
Edited by M.J. Cousins and P.O. Bridenbaugh
**Anaesthesia in hepatic and biliary tract disease** 452
B.R. Brown, Jr
**Intensive care** 453
G.R. Park and A.R. Manara

## Neural blockade in clinical anaesthesia and management of pain, 2nd edn

Edited by M.J. Cousins and P.O. Bridenbaugh. Pp. xix–1171. J.B. Lippincott, 1987. £120.0

This book might be termed a blockbuster, and the increased size of this second edition will enable the lucky owner to bust a lot more blocks than he could with his old one. Seven years have elapsed since the original, with many changes in the use of regional anaesthetic techniques, and these are reflected in the new edition.

It is no longer enough for the crowned heads of regional anaesthesia to make unsupported statements that a particular technique is superior. Critics of regional anaesthesia are demanding proof in the form of basic science and controlled clinical trials. The editors have answered this with a wholesale revision which sees the introduction of no less than 24 new contributors, 'all of whom have played a key role in the field that is the subject of their chapter'. Tautology apart, this exercise has been successful, with the introduction of a few more household names to provide greater weight to the substantial reputation of this book. The 'key role' that some of the contributors have played escapes this reviewer, but the overall standard in each chapter remains very high, with only an occasional low. This is a risk every editor takes when dealing with household names, as many will have long since ceased 'sharp-end' anaesthesia in favour of the suitcase full of slides, the transit lounge and a staple diet of rubber chicken.

The book starts with a splendid introduction to the history of neural blockade by Fink. The extent of the revision is illustrated by the fact even this section has been rewritten and several new references included. Thereafter are sections on pharmacology and physiology, techniques and the use of neural blockade in the management of pain. A large number of the chapters are new. Those that are not have been rewritten extensively and include substantial numbers of new references. All the contributions in the section on pharmacology and physiology are first rate.

Each chapter in the techniques section represents a statement by the author about personal practice. The views and techniques are all worthy of consideration, but should not be regarded as tablets of stone. Thus, it is possible to disagree with some of the practice described. For example, I remain to be convinced of the benefits of using multiple needle techniques for neurolytic lumbar sympathectomy, and would not be especially happy with some of the X rays used for illustration. There are other examples, but the quality and quantity of information provided in every chapter overcomes any minor carping. The chapters on spinal and epidural techniques, those by both Bridenbaughs and that by Murphy are particularly impressive.

The use of neural blockade in the management of pain is undergoing critical reassessment. The simplistic approach, so often reflected in requests from colleagues to 'do a nerve block' is dying a protracted death, and careful consideration of the enlarged section on pain management will speed this process. However, there are still traces of the school of thought that believes a nerve block is the answer to every known ill, thus there is contrast between the carefully argued chapter on diagnostic blockade by Boas and Cousins and succeeding chapters. The problems inherent in the use of diagnostic blockade are illustrated in the chapter by Bogduk who describes the techniques of zygapophysial blocks with meticulous care. Bogduk believes facet syndromes to be common, although others have shown very low response rates to the diagnostic blockade he advocates. Selective overkill in referencing is the preferred method of hammering home the point. Interestingly, another sort of selective referencing can be found later in the same chapter when, surprisingly, there is no reference to the two main reviews of the use of epidural steroids in the consideration of that topic.

Cousins and two of his colleagues at Flinders make a great deal of sense in their review of the use of spinal opioids in acute and chronic pain. This chapter could be read by every examination candidate with benefit. Anaesthetists who remain interested in neurolytic blockade will enjoy the chapter on this subject, but may be mystified by the preceding chapter by Myers and Katz on the neuropathology of neurolytic and semidestructive agents, whatever they are.

In summary, reviewers are asked to indicate the contents, scope, target audience and relevance to the practice of anaesthesia of the book under consideration. Briefly, this book contains 32 chapters that cover the use of neural blockade for anaesthesia and pain relief. They are well edited, splendidly illustrated and exhaustively referenced. The new edition has undergone sufficient revision to constitute a new book and will be useful to anyone with an interest in this subject and provides insight for those that do not. Despite the price, department libraries and individuals will find this book good value and I recommend it.

J.E. Charlton

## Anaesthesia in hepatic and biliary tract disease

B.B. Brown, Jr. Pp. xxi + 300. F.A. Davis, 1988. $72.50.

Most anaesthetists will recognise Professor Burnell Brown as an anaesthetist who had published a number of papers relating to the liver and anaesthesia. Perhaps, like me, they did not know that his knowledge (and experience) was so broad. Like myself, I believe that many anaesthetists, profess only a modicum of knowledge related to hepatology. I therefore opened this book with both keenness and a sense of foreboding (about how little I might know). I went straight to the chapter on pulmonary (and cardiovascular) consequences of liver disease. My forebodings were correct: my ignorance was being shown up. I therefore read this book with care: it did not seem to be one for flicking through.

The book is divided into five major sections, each containing a varying number of chapters. The sections deal with fundamental principles (anatomy and physiology), the effects of anaesthesia on the liver, the problems of liver disease for the anaesthetist, biliary tract disease, and special problems such as postoperative jaundice. Each chapter stands on its own: there is relatively little cross referencing, but as might be expected from a single author book, there is little repetition.

Initially, I found the author's style discursive, and indeed heavy going. However, each chapter ends with a fairly concise summary, and the simple expedient of reading the summary first, made the whole chapter much easier to follow. Each chapter is peppered with nicely drawn tables or diagrams. The manner is that of the popular 'Medicine International' series, with what amounts to learning points on each page. Inevitably the occasional table was overleaf from the relevant text. In the future, these tables will act as my excellent quick reference guide to the problems of liver disease.

It is obvious from the text that the author has vast practical experience of anaesthesia in 'hepatic' patients. His comments (negative!) concerning the physician's demand for tracheal intubation prior to insertion of a Sengstaken tube (necessary to prevent vomiting and aspiration during insertion of the Sengstaken tube!) conjures up an interesting picture of the bedside discussion with the hepatologist.

Other than the second chapter (very simple anatomy), I had little to quarrel with in this book, apart from a few text errors. The references were wide ranging, selective, and up to date (1987) and followed each chapter. The index was usefully long.

This book should be purchased by postgraduate libraries. If available as a reference book in anaesthetic departments, the tables of learning points will keep most anaesthetists, including myself, out of trouble.

Professor Brown points out in his preface that while there is an almost overwhelming interest in anaesthesia and the cardiopulmonary system, he believes the hepatic patient to be more at risk from anaesthesia and surgery than the cardiac patient. The contents of this monograph make me inclined to agree with him.

P.G. Lawler

### Intensive care

G.R. Park and A.R. Manara. Pp 299. Castle House, 1988. £12.95

This useful little book has been written with the ITU resident in mind but may well find favour with other medical staff, nurses and medical students. It is also a useful quick reference for more senior staff. This soft-backed, pocket-sized book is divided into two main sections.

The first deals in brief with causes, diagnosis, investigation and management of various common intensive care disorders. Here there is much information, but unfortunately it is not as well ordered as might be and this is my main criticism. For example, the chapters on cardiopulmonary resuscitation and on shock both fail adequately to emphasise the importance of oxygenation. Administration of oxygen in the chapter on shock, is placed third on a list of things to do after intravenous access and institution of monitoring. Oxygen therapy warrants only sixth place in the myocardial infarction section whilst for congestive cardiac failure it is listed only as an additional measure. Much emphasis is placed on sodium bicarbonate therapy when perhaps this should be played down somewhat.

The chapter on common respiratory problems opens with a discussion on ARDS. Is this really a common respiratory disorder? The discussion on chest injuries suggests that if ventilation proves necessary for a flail chest it is usually needed for 10–14 days. This is classical teaching but not present practice. CPAP is not mentioned in this context. Apart from these problems the reader is well served in section 1.

Section 2 briefly describes 11 practical procedures which range from tracheal intubation through cardiac pacing to haemofiltration. This works well as a supplement to learning the techniques under supervision but I wonder who will read the chapter on tracheal intubation?

These criticisms should not be overemphasised. The book is good value and will become a success. I look forward to the second edition which one hopes will provide the junior with the priorities of basic intensive care more logically ordered.

E. Major

*Anaesthesia*, 1989, Volume 44, pages 454–458

# Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for January 1989. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

## Abdominal surgery

Effect of continuous postoperative epidural analgesia on intestinal motility. Ahn H, Bronge A *et al. British Journal of Surgery* 1988; **75:** 1176.

Regulation of gastrointestinal function by multiple opioid receptors. Burks TF, Fox DA *et al. Life Sciences* 1988; **43:** 2177.

Gastrointestinal gas. Fardy J, Sullivan S. *Canadian Medical Association Journal* 1988; **139:** 1137.

Endogenous and exogenous opioids in the control of gastrointestinal motility and secretion. Kromer W. *Pharmacological Reviews* 1988; **40:** 121.

Glucagon selectively increases splanchnic blood flow in patients with well compensated cirrhosis. Lee SS, Moreau R *et al. Hepatology* 1988; **8:** 1501.

Cisapride: A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in gastrointestinal motility disorders. McCallum RW, Prakash C *et al. Drugs* 1988; **36:** 652.

Comparison of the effect of cisapride and metoclopramide on morphine-induced delay in gastric emptying. Rowbotham DJ, Bamber PA, Nimmo WS. *British Journal of Clinical Pharmacology* 1988; **26:** 741.

Perioperative blood transfusions are associated with decreased time to recurrence and decreased survival after resection of colorectal liver metastases. Stephenson KR, Steinberg SM *et al. Annals of Surgery* 1988; **208:** 679.

The physiology of gastric acid secretion. Wolfe MM, Soll AH. *New England Journal of Medicine* 1988; **319:** 1707.

## Pharmacology

### *Adrenergic drugs and their antagonists*

Support for adrenaline-hypertension hypothesis: 18 hour pressor effect after 6 hours adrenaline infusion. Blankestijn PJ, Man In't Veld AJ *et al. Lancet* 1988; **2:** 1386.

Propranolol enhances adenine nucleotide degradation in human muscle during exercise. Broberg S, Katz A, Sahlin K. *Journal of Applied Physiology* 1988; **65:** 2478.

Epinephrine potentiates human platelet activation but is not an aggregating agent. Lanza F, Beretz A *et al. American Journal of Physiology* 1988; **255** (No. 6 Part 2): H1276.

### *Anaesthetic agents*

Anaesthetic potencies of primary alkanols: implications for the molecular dimensions of the anaesthetic site. Alifimoff JK, Firestone LL, Miller KW. *British Journal of Pharmacology* 1989; **96:** 9.

Respiratory center output following zopiclone or diazepam administration in patients with pulmonary disease. Beaupre A, Soucy R *et al.* In: Levivalensi P, Duron B, eds. *Sleep disorders and respiration.* Paris: Inst. Natl. Sante Recherche Medicale, 1988: 123.

Steroidal modulation of the GABAa-benzodiazepine receptor complex—an electrophysiological investigation. Lambert JJ, Peters JA. In: Barnard EA, Costa E, eds. *Allosteric modulation of amino acid receptors: therapeutic implications.* New York: Raven Press, 1989: 139.

Halothane hepatitis. Neuberger J. *ISI Atlas of Science—Pharmacology* 1988; **2:** 309.

Halothane hepatitis—a model of immunoallergic disease. Neuberger J, Kenna JG. In: Guillouzo A, ed. *Liver cells and drugs.* Paris: Inst. Natl. Sante Recherche Medicale, 1988: 161.

Acute effects of amitriptyline on human performance and interactions with diazepam. Patat A, Klein MJ *et al. European Journal of Clinical Pharmacology* 1988; **35:** 585.

A physiologically based pharmacokinetic model for inhaled carbon tetrachloride. Paustenbach DJ, Clewell HJ III *et al. Toxicology and Applied Pharmacology* 1988; **96:** 191.

### *Analgesic agents*

Decrease in analgesic effect of nifedipine following chronic morphine administration. Ohnishi T, Saito K *et al. European Journal of Pharmacology* 1988; **158:** 173.

Morphine can stimulate prolactin release independent of a dopaminergic mechanism. Shin SH, Obonsawin MC *et al. Canadian Journal of Physiology and Pharmacology* 1988; **66:** 1381.

### *Muscle relaxants*

Metabolic and circulatory responses to normoxic skeletal muscle to whole-body hypoxia. Bredle DL, Chapler CK, Cain SM. *Journal of Applied Physiology* 1988; **65:** 2063.

Train-of-four fade during neuromuscular blockade induced by tubocurarine, succinylcholine or a-bungarotoxin in the rat isolated hemidiaphragm. Cheah LS, Gwee MCE. *Clinical and Experimental Pharmacology and Physiology* 1988;.**15:** 937.

Mechanisms resisting fatigue in isometrically contracting human skeletal muscle. Gibson H, Cooper RG *et al. Quarterly Journal of Experimental Physiology* 1988; **73:** 903.

Response of muscle spindles depend on their history of activation and movement. Gregory JE, Morgan DL, Proske U. In: Hamann W, Iggo A, eds. *Transduction and cellular mechanisms in sensory receptors.* Amsterdam: Elsevier, 1988: 85.

Molecular structure and function of acetylcholine receptors and sodium channel. Numa S. In: Chien S, ed. *Molecular biology in physiology.* New York: Raven Press, 1989: 93.

### *Other drugs*

Guide to drug dosage in hepatic disease. Bass NM, Williams RL. *Clinical Pharmacokinetics* 1988; **15:** 396.

Guid to drug dosage in renal failure. Bennett WM. *Clinical Pharmacokinetics* 1988; **15:** 326.

Humoral effects of metoclopramide and domperidone in normal subjects and in hypertensive patients. Bernini GP, Lucarini AR *et al. Journal of Endocrinological Investigation* 1988; **11:** 711.

Disposition of a flow-limited drug (lidocaine) and a metabolic capacity-limited drug (theophylline) in liver cirrhosis. Colli A, Buccino G *et al. Clinical Pharmacology and Therapeutics* 1988; **44:** 642.

---

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Drug metabolism in liver disease. Howden CW, Birnie GG, Brodie MJ. *Pharmacology and Therapeutics* 1989; **40:** 439.

Hepatic drug disposition in multiple organ failure. Schregel W, Kuntz HD, Vitt M. *Acta Anaesthesiologica Scandinavica* 1988; **32:** 638.

Pharmacologic methods for identification of receptors. Tallarida RJ. *Life Sciences* 1988; **43:** 2169.

## Apparatus

A new method for the classification of subvigil stages, using the Fourier transform, and its application to sleep apnea. Penzel T, Petzold J. *Computers in Biology and Medicine* 1989; **19:** 7.

Arterial $O_2$ saturation during Nd-YAG laser photoresection of endobronchial tumors under LA—use of intermittent $O_2$ with pulse oximetry guidance. Schiffman PL, Wilhelm J, Prisi RA. *Chest* 1988; **94:** 1300.

## Complications

Cardiac arrest during anaesthesia—a computer-aided study in 250-543 anaesthetics. Olsson GL, Hallen B. *Acta Anaesthesiologica Scandinavica* 1988; **32:** 653.

Mechanisms of drug-induced hepatitis. Pessayre D, Larrey D. In: Guillouzo A, ed. *Liver cells and drugs*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 129.

Forms of hepatic failure in patients with liver cirrhosis. Watanabe A, Nagashima H. *Journal of Medicine* 1988; **19:** 383.

## General anaesthetic procedures

Difficult laryngoscopy and diabetes mellitus. Hogan K, Rusy D, Springman SR. *Anesthesia and Analgesia* 1988; **67:** 1162.

Gastric fluid volume, pH, and emptying in elective in patients. Influences of narcotic-atropine premedication, oral fluid, and ranitidine. Maltby JR, Koehli N *et al. Canadian Journal of Anaesthesia* 1988; **35:** 562.

Detection of interruptions in the breathing gas of ventilated anaesthetized patients. McEwen JA, Small CF, Jenkins LC. *Central Journal of Anaesthesia* 1988; **35:** 549.

## General interest

The human sphincter of Oddi—physiology and pathophysiology. Goff JS. *Archives of Internal Medicine* 1988; **148:** 2673.

## Local analgesia

Local analgesic techniques for upper abdominal surgery—endocrine and metabolic effects. Hall GM, Cacoumenta S. *British Journal of Anaesthesia* 1988; **61:** 649.

## Spinal opioids

Opioid peptides and neuroendocrine function in man. Grossman A. In: Imura ed. *Neuroendocrine control of the hypothalamo-pituitary system*. Tokyo: Japan Sci. Soc. Press, 1988: 93.

Review: opioids and stress in man. Grossman A. *Journal of Endocrinology* 1988; **119:** 377.

Reversal of epidural morphine induced respiratory depression and pruritus with nalbuphine. Penning JP, Samson B, Baxter AD. *Canadian Journal of Anaesthesia* 1988; **35:** 599.

Effect of kappa-opioid receptor agonists on morphine analgesia in morphine-naive and morphine-tolerant rats. Ramarao P, Jablonski HI Jr *et al. European Journal of Pharmacology* 1988; **156:** 239.

## Obstetric anaesthesia and analgesia

Short-term effects of maternal oxygen administration on blood flow velocity waveforms in healthy and growth-retarded fetuses. Arduini D, Rizzo G *et al. American Journal of Obstetrics and Gynecology* 1988; **159:** 1077.

Maternal physiologic adaptations to early human pregnancy. Clapp JF III, Seaward BL *et al. American Journal of Obstetrics and Gynecology* 1988; **159:** 1456.

Influence of bupivacaine as an adjuvant to epidural morphine for analgesia after cesarean section. Douglas MJ, McMorland GH, Janzen JA. *Anesthesia and Analgesia* 1988; **67:** 1138.

The effect of pregnancy on drug pharmacokinetics. Jeffries WS, Bochner F. *Medical Journal of Australia* 1988; **149:** 675.

Nocturnal positive-pressure nasal ventilation for respiratory failure during pregnancy. McKim DA, Dales RE *et al. Canadian Medical Association Journal* 1988; **139:** 1069.

Preeclampsia: a microvesicular fat disease of the liver? Minakami H, Oka N *et al. American Journal of Obstetrics and Gynecology* 1989; **150:** 1043.

A successful program to lower cesarean-section rates. Myers SA, Gleicher N. *New England Journal of Medicine* 1988; **319:** 1511.

Increased ventilation requirements during obstetric general anaesthesia. Rampton AJ, Mallaiah S, Garrett CPO. *British Journal of Anaesthesia* 1988; **61:** 730.

Low-dose aspirin. 1. Effect on angiotension II pressor response and blood prostaglandin concentrations in pregnant women sensitive to angiotensin II. Spitz B, Magness RR *et al. American Journal of Obstetrics and Gynecology* 1988; **159:** 1035.

Dexamethasone effects on ritodrine-induced changes in myometrial contractility and beta-adrenergic receptor function. Ward SM, Caritis SN *et al. American Journal of Obstetrics and Gynecology* 1988; **159:** 1461.

Severe Takayasu's arteritis in pregnancy: the role of central hemodynamic monitoring. Winn HN, Setaro JF *et al. American Journal of Obstetrics and Gynecology* 1988; **159:** 1135.

## Paediatric anaesthesia and intensive care

Optimizing ventilatory settings using pulse oximetry in the transition between life and death. Andersen JB. *Scandinavian Journal of Clinical and Laboratory Investigation* 1988; **48** (Suppl. 189): 59.

Effects of sleep deprivation on respiration during sleep in healthy infants. Canet E, Gaultier C *et al.* In: Levivalensi P, Duron B eds. *Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 37.

Differences in $CO_2$ threshold of respiratory muscles in preterm infants. Carlo WA, Martin RJ, Difiore JM. *Journal of Applied Physiology* 1988; **65:** 2434.

Fetal hypoxia elevates plasma atrial natriuretic factor concentration. Cheung CY, Brace RA. *American Journal of Obstetrics and Gynecology* 1988; **159:** 1263.

The oxygen-base and acid-base status during hypothermic cardiopulmonary bypass. Gothgen IH, Siggaardandersen O *et al. Scandinavian Journal of Clinical and Laboratory Investigation* 1988; **43** (Suppl. 189): 63.

Poor reversibility of EEG abnormality in hypotensive, preterm neonates. Greisen G, Pryds O *et al. Acta Paediatrica Scandinavica* 1988; **77:** 785.

Gestational effects of corticosteroids and surfactant in ventilated rabbits. Ikegami M, Jobe AH *et al. Pediatric Research* 1989; **25:** 32.

Complications of anaesthesia in infants and children. Leading Article. *Lancet* 1988; **2:** 1466.

Noninvasive monitoring of blood gases in the neonatal period. Lindemann R, Haga P *et al. Scandinavian Journal of Clinical and Laboratory Investigation* 1988; **48** (Suppl. 189): 33.

Autonomic modulation of fetal atrial natriuretic factor and urine flow responses to vascular volume expansion. Liner LK, Cheung CY, Brace RA. *American Journal of Obstetrics and Gynecology* 1988; **159:** 1341.

Transcutaneous $Po_2$—monitoring in neonates with bronchopulmonary dysplasia. Markestad T. *Scandinavian Journal of Clinical and Laboratory Investigation* 1988; **48** (Suppl. 189): 37.

Surfactant replacement. Merritt TA, Hallman M. *American Journal of Diseases of Children* 1988; **142:** 1333.

The effects of magnesium sulfate therapy on Apgar scores. Pruett KM, Kirshon B *et al. American Journal of Obstetrics and Gynecology* 1988; **159:** 1047.

Surfactant metabolism during hyperventilation of newborn lambs with atrial right to left shunts. Rider ED, Jobe AH *et al. Pediatric Research* 1989; **25:** 83.

The effect of diazepam on neonatal seizure: *in vivo* 31P and 1H NMR study. Young RSK, Chen B *et al. Pediatric Research* 1989; **25:** 27.

## Cardiovascular system

### *Physiology*

Atrial natriuretic factor attenuates the pulmonary pressor response to hypoxia. Adnot S, Chabrier PE *et al. Journal of Applied Physiology* 1988; **65:** 1975.

Metabolic and ionic changes in muscle during hemorrhagic shock. Blum H, Schnall MD *et al. Circulatory Shock* 1988; **26:** 341.

Carotid sinus baroreceptor control of splanchnic resistance and capacity. Brunner MJ, Greene AS *et al. American Journal of Physiology* 1988; **255** (No. 6 Part 2): H1305.

Altered calcium homeostasis in the pathogenesis of myocardial ischemic and hypoxic injury. Buja LM, Hagler HK, Willerson JT. *Cell Calcium* 1988; **9:** 205.

The absence of cardiovascular and respiratory responses to changes in right ventricular pressure in anaesthetized dogs. Crisp AJ, Hainsworth R, Tutt SM. *Journal of Physiology* 1988; **407:** 1.

Toxicological aspects of liver heme biosynthesis. De Matteis F. *Seminars in Hematology* 1988; **25:** 321.

Calcium channel binding characteristics in the human heart. Finkel MS, Patterson RE *et al. American Journal of Cardiology* 1988; **62:** 1281.

Sequential neurohumoral measurements in patients with congestive heart failure. Francis GS, Rector TS, Cohn JN. *American Heart Journal* 1988; **116** (No. 6 Part 1): 1464.

Arterial hypertension is associated with hypalgesia in humans. Ghione S, Rosa C *et al. Hypertension* 1988; **12:** 491.

Effects of hypoxia and reoxygenation on maximum rate of early left ventricular filling. Kusunoki K, Nakamura Y *et al. American Journal of Physiology* 1988; **255** (No. 6 Part 2): H1311.

Oxygen consumption and coronary reactivity in postischemic myocardium. Laxson DD, Homans DC *et al. Circulation Research* 1989; **64:** 9.

Atrial natriuretic hormone has biological effects in man at physiological plasma concentrations. Richards AM, McDonald D *et al. Journal of Clinical Endocrinology and Metabolism* 1988; **67:** 1134.

Regulation of the coagulation system by vascular endothelial cells. Stern DM, Kaiser E, Nawroth PP. *Haemostasis* 1988; **18:** 202.

### *Treatment and medication*

The relationship between pharmacokinetics and pharmacodynamics of enoximone in healthy man. Belz GG, Meinicke T, Schaferkorting M. *European Journal of Clinical Pharmacology* 1988; **35:** 631.

Ketanserin in the treatment of diabetes-associated hypertension. Beretta-Piccoli C. *Drugs* 1988; **36** (Suppl. 1): 35.

Captopril: an update of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in hypertension and congestive heart failure. Brogden RN, Todd PA, Sorkin EM. *Drugs* 1988; **36:** 540.

Interaction between digoxin and propafenone. Calvo MV, Martin-Suarez A *et al. Therapeutic Drug Monitoring* 1989; **11:** 10.

Kinetics, dynamics, and bioavailability of bumetanide in healthy subjects and patients with congestive heart failure. Cook JA, Smith DE *et al. Clinical Pharmacology and Therapeutics* 1988; **44:** 487.

Therapeutic reviews: fundamentals of calcium channel blockers. Das G. *International Journal of Clinical Pharmacology, Therapy and Toxicology* 1988; **26:** 575.

Effect of acute administration of propranolol and atenolol on baroreflex function in normal man. Deering AH, Harron DWG *et al. European Journal of Clinical Pharmacology* 1988; **35:** 607.

The relevance of serotonin antagonism in the treatment of hypertension. Doyle AE. *Drugs* 1988; **36** (Suppl. 1): 67.

Nisoldipine: A preliminary review of its pharmacodynamic and pharmacokinetics properties in the treatment of hypertension and related CV disorders. Friedel HA, Sorkin EM. *Drugs* 1988; **36:** 682.

Properties of labetalol, a combined alpha- and beta-blocking agent, relevant to the treatment of myocardial ischemia. Frishman WH. *Cardiovascular Drugs and Therapy* 1988; **2:** 343.

Advantage of combined therapy with captopril and nitrates in severe congestive heart failure. Halon DA, Rosenfeld T *et al. Israel Journal of Medical Sciences* 1988; **24:** 664.

Unstable angina: current concepts of medical management. Hamm CW, Bleifeld W. *Cardiovascular Drugs and Therapy* 1988; **2:** 333.

Hormonal and renal effects of atrial natriuretic peptide in patients with secondary hypertension. Hirata Y *et al. Circulation* 1988; **78:** 1401.

Effects of alpha-human atrial natriuretic peptide on the interrelationship of arterial pressure, aortic nerve activity, and aortic diameter. Hirooka Y, Takeshita A *et al. Circulation Research* 1988; **63:** 987.

Amiodarone alters thyroxine transfer and distribution in humans. Kaptein EM, Egodage PM *et al. Metabolism—Clinical and Experimental* 1988; **37:** 1107.

Angiotensin converting enzyme inhibitors. I. Pharmacology. Kostis JB. *American Heart Journal* 1988; **116** (No. 6 Part 1): 1580. Angiotensin in converting enzyme inhibitors. II. Clinical use. Kostis, JB. *American Heart Journal* 1988; **116** (No. 6 Part 1): 1591.

Percutaneous transluminal coronary angioplasty improves survival in acute myocardial infarction complicated by cardiogenic shock. Lee L, Bates ER *et al. Circulation* 1988; **78:** 1345.

Long-segment coronary ulcerations in survivors of sudden cardiac death. Lo Y-S A, Cutler JE *et al. American Heart Journal* 1988; **116:** (No. 6 Part 1): 1444.

Encainide for treatment of atrioventricular reciprocating tachycardia in the Wolff–Parkinson–White syndrome. Miles WM, Zipes DP *et al. American Journal of Cardiology* 1988; **62** (No. 19): L20.

Doxazosin: a newly developed, selective alpha 1-inhibitor in the management of patients with pheochromocytoma. Miura Y, Yoshinaga K. *American Heart Journal* 1988; **116** (No. 6 Part 2): 1785.

Coagulation changes during packed red cell replacement of major blood loss. Murray DJ, Olson J *et al. Anesthesiology* 1988; **69:** 839.

Advances in the treatment of supraventricular tachycardia—introduction. Naccarelli GV, Wellens HJJ. *American Journal of Cardiology* 1988; **62** (No. 19): L1.

Pharmacokinetics of calcium antagonists. Reid JL, Meredith PA *et al. Journal of Cardiovascular Pharmacology* 1988; **12** (Suppl. 7): S22.

Encainide and related new antiarrhythmic drugs. Roden DM. *ISI Atlas of Science—Pharmacology* 1988; **2:** 374.

Inducible ventricular arrhythmias and sudden death during vasodilator therapy of severe heart failure. Stevenson WG, Stevenson LW *et al. American Heart Journal* 1988; **116** (No. 6 Part 1): 1447.

Initial blood pressure as a predictor of the response to antihypertensive therapy. Sumner DJ, Meredith PA *et al. British Journal of Clinical Pharmacology* 1988; **26:** 715.

Drug therapy: converting-enzyme inhibitors in the treatment of hypertension. Williams GH. *New England Journal of Medicine* 1988; **319:** 1517.

## Respiration

### *Physiology*

Effect of chronic renal failure on respiratory muscle strength. Bark H, Heimer D *et al. Respiration* 1988; **54:** 153.

Effect of hypoxia on diaphragm blood flow, oxygen uptake, and contractility. Bark H, Supinski G *et al. American Review of Respiratory Disease* 1988; **138:** 1535.

Drugs, sleep and breathing. Block AJ. In: Levivalensi P, Duron B, eds. *Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 91.

How accurate are ventilation-perfusion scans for pulmonary embolism? Carracci BF, Rumbolo PM *et al. American Journal of Surgery* 1988; **156:** 477.

Role of $CO_2$ responsiveness and breathing efficiency in determining exercise capacity of patients with chronic airway obstruction. Chonan T, Hida W *et al. American Review of Respiratory Disease* 1988; **138:** 1488.

Sleep apnea syndrome and systemic hypertension. Coccagna G, Lugaresi E, Cirignotta F. In: Levivalensi P, Duron B, eds.

*Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 155.

Paths of ion transport across canine fetal tracheal epithelium. Cotton CU, Boucher RC, Gatzy JT. *Journal of Applied Physiology* 1988; **65:** 2383.

Mechanism of pulmonary function changes after surgical correction for funnel chest. Derveaux L, Ivanoff I *et al. European Respiratory Journal* 1988; **1:** 823.

$O_2$ cost of inspiratory and expiratory resistive breathing in humans. Dodd DS, Yarom J *et al. Journal of Applied Physiology* 1988; **65:** 2518.

The lung volume at which shunting occurs with inhalation anesthesia. Dueck R, Prutow RJ *et al. Anesthesiology* 1988; **69:** 854.

The eripheral-chemoreceptor threshold to carbon dioxide in man. Duffin J, McAvoy GV. *Journal of Physiology* 1988; **406:** 15.

Respiration during sleep on healthy subjects. Duron B. In: Levivalensi P, Duron B, eds. *Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 19.

Hypoxia during sleep in COPD patients. Flenley DC. In: Levivalensi P, Duron B eds. *Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 251.

Role of pulmonary diseases and physical condition in the regulation of vasoactive hormones. Hietanen E, Marniemi J *et al. Clinical Physiology* 1988; **8:** 581.

Regulation of respiratory motor outflow to the larynx and diaphragm by GABA receptors. Holtman JR Jr, King KA. *European Journal of Pharmacology* 1988; **156:** 181.

Palate and hypopharynx—sites of inspiratory narrowing of the upper airway during sleep. Hudgel DW, Hendricks C. *American Review of Respiratory Disease* 1988; **138:** 1542.

The influence of the epidermal membrane on percutaneous $Po_2$ and metabolic rate. Jaszczak P, Sejrsen P, Sorensen PR. *Scandinavian Journal of Clinical and Laboratory Investigation* 1988; **48** (Suppl. 189): 17.

Relative hysteresis of the airways and lung parenchyma in normal subjects. Katz I, Zamel N *et al. Journal of Applied Physiology* 1988; **65:** 2390.

Ventilation inhomogeneity during controlled ventilation. Which index should be used? Larsson A, Jonmarker C, Werner O. *Journal of Applied Physiology* 1988; **65:** 2030.

Effect of hemodilution on ventilatory fluctuations of pulmonary capillary blood volume. Lee JS, Lee LP. *Journal of Applied Physiology* 1988; **65:** 2571.

Comparison of sleep pattern, arterial $O_2$ saturation, ventilatory and heart rate during sleep in humans at sea level and high altitude. Raynaud J, Barragan M *et al.* In: Levivalensi P, Duron B, eds. *Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 39.

Lobar contribution to VA/Q inequality during constant-flow ventilation. Schumacker PT, Solway J *et al. Journal of Applied Physiology* 1988; **65:** 2132.

Cough capacity in patients with muscular dystrophy. Szeinberg A, Tabachnik E *et al. Chest* 1988; **94:** 1232.

Sleep apnea syndrome and metabolic acidosis—a coincidental association. Tardif C, Nouvet G, Verdurepoussin A. In: Levivalensi P, Duron B, eds. *Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 191.

Respiratory sensation and pattern of respiratory muscle activation during diaphragm fatigue. Ward ME, Eidelman D *et al. Journal of Applied Physiology* 1988; **65:** 2181.

### *Treatment and medication*

Regional distribution of ventilation in chronic obstructive lung disease and the effect of salbutamol. Bell D, Kirby TP *et al. Respiration* 1988; **54:** 179.

Severe acute respiratory failure managed with continuous positive airway pressure and partial extracorporeal $CO_2$ removal by an artificial membrane lung. Borelli M, Kolobow T *et al. American Review of Respiratory Disease* 1988; **138:** 1480.

Theophylline and diaphragmatic contractility—investigation of a dose-response relationship. Foxworth JW, Reisz GR *et al. American Review of Respiratory Disease* 1988; **138:** 1532.

Control of breathing in patients with short-term primary hypothyroidism. Gorini M, Spinelli A *et al. Lung* 1989; **167:** 43.

Oxygen uptake during weaning from mechanical ventilation. Hubmayr RD, Loosbrock LM *et al. Chest* 1988; **94:** 1148.

Bronchial responsiveness, lung mechanics, gas transfer, and corticosteroid response in patients with chronic airflow obstruction. James AL, Finucane KE *et al. Thorax* 1988; **43:** 916.

Treatment of the obstructive sleep apnea syndrome using a nasopharyngeal tube. Nahmias JS, Karetzky MS. *Chest* 1988; **94:** 1142.

Home mechanical ventilation. Peters SG, Viggiano RW. *Mayo Clinic Proceedings* 1988; **63:** 1208.

Theophylline pharmacokinetics in normal elderly subjects. Shin S-G, Juan D, Rammohan M. *Clinical Pharmacology and Therapeutics* 1988; **44:** 522.

A 72-year-old man with a history of the nephrotic syndrome and more recent marked edema, dyspnea, and orthopnea. Vlahakes GJ, Southern JF. *New England Journal of Medicine* 1988; **319:** 1592.

Somatostatin in the control of respiration. Yamamoto Y, Runold M *et al. Acta Physiologica Scandinavica* 1988; **134:** 529.

## Central nervous system

### *Physiology*

Acute cerebral ischaemia: concurrent changes in cerebral blood flow, energy metabolites, pH, and lactate. III. Changes following ischaemia. Allen K, Busza AL *et al. Journal of Cerebral Blood Flow and Metabolism* 1988; **8:** 816.

Biological differences between ischemia, hypoglycemia, and epilepsy. Auer RN, Siesjo Bo K. *Annals of Neurology* 1988; **24:** 699.

Reoxygenation and calcium-induced cerebroarterial contractions as affected by vasodilator agents. Bian KA, Toda N. *Journal of Cerebral Blood Flow and Metabolism* 1988; **8:** 808.

Neurotransmitters and modulators in the cerebellum. Kimura H. *Folia Pharmacologica Japonica* 1988; **92:** 337.

Brain transections demonstrate the central origin of hypoxic ventilatory depression in carotid body-denervated rats. Martin-Body RL. *Journal of Physiology* 1988; **407:** 41.

Neuropsychological disturbances and sleep disorders in COPD patients. Pedinielli JL, Campoli C *et al.* In: Levivalensi P, Duron B, eds. *Sleep disorders and respiration*. Paris: Inst. Natl. Sante Recherche Medicale, 1988: 275.

Hyperglycemia is a stress response in acute stroke. Woo E, Ma JTC *et al. Stroke* 1988; **19:** 1359.

### *Treatment and medication*

Use of mannitol during neurosurgery—interpatient variability in the plasma and CSF levels. Anderson P, Boreus L *et al. European Journal of Clinical Pharmacology* 1988; **35:** 643.

Effect of lidocaine after experimental cerebral ischemia induced by air embolism. Evans DE, Catron PW *et al. Journal of Neurosurgery* 1989; **79:** 97.

Esmolol for the control of hypertension after neurologic surgery. Gibson BE, Black S. *et al. Clinical Pharmacology and Therapeutics* 1988; **44:** 650.

Muscle function and morphology in myotonic dystrophy. Grimby G, Hedberg M *et al. Acta Medica Scandinavica* 1988; **224:** 349.

Sleep apnea and hypothyroidism—mechanisms and management. Grunstein RR, Sullivan CE. *American Journal of Medicine* 1988; **85:** 775.

Use of implantable pumps for central nervous system drug infusions to treat neurological disease. Harbaugh RE, Saunders RL, Reeder RF. *Neurosurgery* 1988; **23:** 693.

Predictors of stroke in the elderly. Himmelmann A, Hansson L *et al. Acta Medica Scandinavica* 1988; **224:** 439.

Fatal ischaemic brain oedema after early thrombolysis with tissue plasminogen activator in acute stroke. Koudstaal PJ, Stibbe J, Vermeulen M. *British Medical Journal* 1988; **297:** 1571.

Calcium antagonist activity of vinpocetine and vincamine in several models of cerebral ischaemia. Lamar J-C, Poignet H *et al. Drug Development Research* 1988; **14:** 297.

Long-term outcome for obstructive sleep apnea syndrome patients—mortality. Partinen M, Jamieson A, Guilleminault C. *Chest* 1988; **94:** 1200.

Parkinsonism and the anaesthetist. Severn AM. *British Journal of Anaesthesia* 1988; **61:** 761.

## Endocrine and metabolic

### *Physiology*

Plasma renin activity and aldosterone in untreated hypothyroidism. Arlot S, Mesmacque JD *et al. Hormone and Metabolic Research* 1988; **20:** 720.

Control of release of vasopressin by neuroendocrine reflexes. Bisset GW, Chowdrey HS. *Quarterly Journal of Experimental Physiology*; 1988; **73:** 811.

Potassium and tissue excitability. Clapham DE. In: Seldin DW, Giebisch G, eds. *Regulation of potassium balance.* New York: Raven Press, 1989: 57.

Hepatic metabolism of insulin. Duckworth WC, Hamel FG, Peavy DE. *American Journal of Medicine* 1988; **85:** 71.

Endocrine aspects of obesity. Glass AR. *Medical Clinics of North America* 1989; **73:** 139.

Blood flow in diabetics with foot lesions due to 'small vessel disease'. Irwin ST, Gilmore J *et al. British Journal of Surgery* 1988; **75:** 1201.

Neural control of renal circulation. Kon V. *Mineral and Electrolyte Metabolism* 1989; **15:** 33.

Clinical diagnosis of abnormal potassium balance. Linas SL, Berl T. In: Seldin DW, Giebisch G, eds. *Regulation of potassium balance.* New York: Raven Press, 1989: 177.

Renal perfusion/reperfusion injuries. McDougal WS. *Journal of Urology* 1988; **140:** 1325.

Influence of norepinephrine administration upon pituitary hormone secretion in normal men. Mileikowsky GN, Farmer RM *et al. Journal of Endocrinological Investigation* 1988; **11:** 641.

Adrenal renin: a possible local hormonal regulator of aldosterone production. Mulrow PJ *et al. Cardiovascular Drugs and Therapy* 1988; **2:** 463.

Vasopressin—physical stress potentiates but emotional stress suppresses its secretion. Onaka T, Yagi K, Hamamura M. In: Imura H, ed. *Neuroendocrine control of the hypothalamo-pituitary system.* Tokyo: Japan Sci. Soc. Press, 1988: 213.

Role of heme in endocrine function. Piper WN. *Seminars in Hematology* 1988; **25:** 330.

Central regulation of stimulus-induced ACTH secretion—characterization of hypophysial-portal plasma CRF and AVP concentration profiles. Plotsky PM. In: Imura H, ed. *Neuroendocrine control of the hypothalamo-Pituitary system.* Tokyo: Japan Sci. Soc. Press; 1988: 31.

Vasoactive intestinal peptide and anterior pituitary function. Prysor-Jones RA, Jenkins JS. *Clinical Endocrinology* 1988; **29:** 677.

Fast cortisol-induced inhibition of the adrenocorticotropin response to surgery in humans. Raff H, Flemma RJ *et al. Journal of Clinical Endocrinology and Metabolism* 1988; **67:** 1146.

Role of insulin resistance in human disease. Reaven GM. *Diabetes* 1988; **37:** 1595.

Potassium deficiency—pathogenesis and treatment. Schuster VL. In: Seldin, DW, Giebisch G, eds. *Regulation of potassium balance.* New York: Raven Press, 1989: 241.

Postoperative diabetes insipidus. Seckl J, Dunger D. *British Medical Journal* 1989; **298:** 2.

Atrial natriuretic hormone effect on renal function and aldosterone secretion in sodium depletion. Shenker Y. *American Journal of Physiology* 1988; **255** (No. 6 Part 2): R867.

Potassium intoxication—pathogenesis and treatment. Stokes JB. In: Seldin DW, Giebisch G, eds. *Regulation of potassium balance.* New York: Raven Press, 1989: 269.

Internal exchanges of potassium. Williams ME, Epstein FH. In: Seldin DW, Giebisch G, eds. *Regulation of potassium blaance.* New York: Raven Press, 1989: 3.

Regulation of porphyrin and heme metabolism in the kidney. Woods JS. *Seminars in Hematology* 1988; **25:** 336.

Hyperinsulinemia. Yalow RS, Rose HG, Bauman WA. *American Journal of Medicine* 1988; **85:** 22.

## Endocrine and metabolic

### *Treatment and medication*

Effects of diuretic drugs on the lipid profile. Ames A. *Drugs* 1988; **36** (Suppl. 2): 33.

Ageing. Serotonin and ketanserin. Breckenridge AM. *Drugs* 1988; **36** (Suppl. 1): 44.

The renal response to low dose dopamine. Schwartz LB, Gewertz BL. *Journal of Surgical Research* 1988; **45:** 574.

Plasma glucose and insulin responses to oral and intravenous glucose in cold-exposed humans. Vallerand AL, Frim J, Kavanagh MF. *Journal of Applied Physiology* 1988; **65:** 2395.

Diuretics and potassium. Wilcox CS. In: Seldin DW, Giebisch G, eds. *Regulation of potassium balance.* New York: Raven Press, 1989: 325.

Suppression of primary and secondary peptides with somatostatin analog in the therapy of functional endocrine tumors. Woltering EA, Mozell EJ *et al. Surgery—Gynecology and Obstetrics* 1988; **167:** 453.

## Pain

### *Physiology*

The relationship between pain drawings and the psychological state. Ginzburg BM, Merskey H, Lau CL. *Pain* 1988; **35:** 141.

Human brain metabolism of morphine and naloxone. Wahlstrom A, Winblad B *et al. Pain* 1988; **35:** 121.

Post-herpetic neuralgia: 208 cases. Watson CPN, Evans RJ *et al. Pain* 1988; **35:** 289.

### *Treatment and medication*

Epidural morphine delivered by a percutaneous epidural catheter for outpatient treatment of cancer pain. Downing JE, Busch EH, Stedman PM. *Anesthesia and Analgesia* 1988; **67:** 1159.

Intractable pain: a neglected area of medical education in the UK. Marcer D, Deighton S. *Journal of the Royal Society of Medicine* 1988; **81:** 698.

Nimesulide: A preliminary review of its pharmacological properties and therapeutic efficacy in inflammation and pain states. Ward A, Brogden RN. *Drugs* 1988; **36:** 732.

## Other

### *Treatment and medication*

Preoperative transfusions in transplantation. Corry RJ, Hunsicker LG. *Transplantation Proceedings* 1988; **20:** 1074.

*Anaesthesia*, 1989, Volume 44, page 459

# Stop Press

## Hazard HC(Hazard) (89) 6, 20 February 1989

### Ohmeda, Excel anaesthetic machines: valve malfunction

The Department of Health has received reports in which the anaesthetic gas being delivered to the patient was unintentionally diluted with excess oxygen. This could result in the patient not being fully anaesthetised and becoming aware.

Users of the Excel range of anaesthetic machines should be extra vigilant. An oxygen analyser, in the breathing system, must be used at all times. If any discrepancy is seen the equipment must be withdrawn from use, and the Department of Health and Ohmeda should be notified immediately.

A diaphragm in a valve is faulty and *all* machines must be inspected by Ohmeda.

# International congress calendar

**1–4 June, 1989.** Baltimore, Maryland, USA. *2nd Annual Trauma Anesthesia and Critical Care Symposium.*

*Information:* Maryland Institute for Emergency Medical Services Systems, 11 South Paca Street, Suite 303, Baltimore, Maryland, USA 21201.

# THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

**Ordinary Membership** (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

**Overseas and Associate Membership**

The right of attendance at the Annual Scientific Meeting and other meetings of the Association.

**Junior Membership** (*United Kingdom and Ireland only*)

Voting membership of the Association.

Representation on the Council of the Association. The Chairman and Secretary of the Junior Group sit on Council as voting members.

Attendance at the Annual Scientific Meeting of the Association and at the special Annual Scientific Meeting of the Junior Anaesthetists' Group, at which Junior Members of the Association are given preference.

**Membership Fees** (inclusive of the journal *Anaesthesia*)

*Ordinary Members:* Subscription **£80** (Husband and wife **£58** each)

*Overseas and Associate Members:* Subscription **£80**

*Junior Members:* Subscription **£45** (**£58** after 3 years if still in training)

*Retired Members:* who receive *Anaesthesia* **£12** (there is no subscription for those who do not).

**How to apply for membership**

Fill in the application form on the other side of this page.

Have it countersigned by two members of the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

**Do not send money with your application**

# THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

**Ordinary Membership** (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

**Overseas and Associate Membership**

The right of attendance at the Annual Scientific Meeting and other meetings of the Association.

**Junior Membership** (*United Kingdom and Ireland only*)

Voting membership of the Association.

Representation on the Council of the Association. The Chairman and Secretary of the Junior Group sit on Council as voting members.

Attendance at the Annual Scientific Meeting of the Association and at the special Annual Scientific Meeting of the Junior Anaesthetists' Group, at which Junior Members of the Association are given preference.

**Membership Fees** (inclusive of the journal *Anaesthesia*)

*Ordinary Members:* Subscription **£80** (Husband and wife **£58** each)

*Overseas and Associate Members:* Subscription **£80**

*Junior Members:* Subscription **£45** (**£58** after 3 years if still in training)

*Retired Members:* who receive *Anaesthesia* **£12** (there is no subscription for those who do not).

**How to apply for membership**

Fill in the application form on the other side of this page.

Have it countersigned by two members of the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

**Do not send money with your application**

*Anaesthesia*, 1989, Volume 44, page 459

# Stop Press

## Hazard HC(Hazard) (89) 6, 20 February 1989

### Ohmeda, Excel anaesthetic machines: valve malfunction

The Department of Health has received reports in which the anaesthetic gas being delivered to the patient was unintentionally diluted with excess oxygen. This could result in the patient not being fully anaesthetised and becoming aware.

Users of the Excel range of anaesthetic machines should be extra vigilant. An oxygen analyser, in the breathing system, must be used at all times. If any discrepancy is seen the equipment must be withdrawn from use, and the Department of Health and Ohmeda should be notified immediately.

A diaphragm in a valve is faulty and *all* machines must be inspected by Ohmeda.

# International congress calendar

**1–4 June, 1989.** Baltimore, Maryland, USA. *2nd Annual Trauma Anesthesia and Critical Care Symposium.*

*Information:* Maryland Institute for Emergency Medical Services Systems, 11 South Paca Street, Suite 303, Baltimore, Maryland, USA 21201.

# FLUID RESUSCITATION

**(Baillières Clinical Anaesthesiology)**

EDITORS: **W. Kox** *Dept Anaesthesia, Charing Cross and Westminster Medical School, London, UK*

**J. Gamble** *Dept Physiology, Charing Cross and Westminster Medical School, London, UK*

THIS practical, research-based reference book not only covers the wide range of topics that need to be addressed during the management of patients in shock, but also considers the rationale for their implementation.

Up-to-date reviews include new approaches in resuscitation, e.g. the development of artificial $O_2$ carriers and the use of low volume hyperosmotic, hyperoncotic resuscitation techniques. The ongoing discussion, crystalloid versus colloid fluid replacement, is considered. The cardiovascular effects of fluid administration as well as the rationale for the use of ionotropic and vasoactive drugs following fluid loading are examined. Likewise, the effect of protein metabolism and fluid balance and its implications on parenteral nutrition during the process of fluid resuscitation is discussed. Problems arising from fluid replacement therapy such as reperfusion injury, the administration of particulate contaminants, plasma substitutes and the interference of these substances with blood grouping are addressed as well as the prevention and treatment of fluid overload. This book caters for the requirements of specialists in intensive care, anaesthetists as well as physicians and surgeons who are interested in understanding and thereby pre-empting shock-related injury.

## Contents

PATHOPHYSIOLOGY AND PRINCIPLES OF FLUID RESUSCITATION:

**J. Gamble** - The principles governing microvasculature transendothelial fluid exchange
**A. Kirkman & R.A. Little** - The pathophysiology of trauma and shock
**S. J. Machin** - Disturbances of haemostasis in surgical and critically ill patients
**M.I.M. Noble** - Cardiovascular response to fluid loading
**J.L. Vincent** - A rationale for the use of inotropic and vasoactive drugs during fluid loading

FLUID REPLACEMENT THERAPY:

**U. Kreimeier & K. Messmer** - Fluid replacement in shock
**W. Shoemaker** - Crystalloid versus colloid fluid resuscitation
**E.S. Parry** - The use of blood products in the treatment of hypovalaemia and shock
**D. Denison** - Artificial oxygen carriers
**A. Fleck** - Nutrition, protein metabolism and fluid balance

SEQUELAE AND SIDE-EFFECTS OF FLUID RESUSCITATION:

**D. Royston** - Reperfusion injury
**W. Kox** - Influence of plasma substitutes on blood typing and cross matching
**H. Hesselvick & B. Brodin** - Reticulo-endothelial response to administration of plasma substitutes
**C.N. McCollum** - The use of microfilters in fluid resuscitation
**T.A. Golper** - Treatment of the overhydrated patient in the ITU

**0 7020 1340 4 ca 230pp Hb June 1989 Baillière Tindall £18.50**

**Baillière Tindall**

**Available from your local bookseller. Prices, specifications and availability are subject to change without prior notice. For further information please contact: Marketing Department, Harcourt Brace Jovanovich Ltd, 24-28 Oval Road, London NW1 7DX, UK.**

# Contents: Anaesthesia, vol. 44, no. 5, May 1989

EDITORIAL

Anaesthesia in old age
*R.M. Jones* 377

ORIGINAL ARTICLES

The effect of acutely administered phenytoin on vecuronium-induced neuromuscular blockade
*H.St.J. Gray, R.M. Slater and B.J. Pollard* 379
Haemodynamic responses to nicardipine in humans anaesthetised with halothane
*D.C. Ray and G.B. Drummond* 382
The effects of speed of injection on induction with propofol. A comparison with etomidate
*G.W.A. Gillies and N.W. Lees* 386
Bed rest and postlumbar puncture headache. The effectiveness of 24 hours' recumbency in reducing the incidence postlumbar puncture headache
*P.T. Cook, M.J. Davies and R.E. Beavis* 389
Gelling of urea-linked gelatin with fresh frozen plasma
*F. Murray and P. Hutton* 392
Effect of buprenorphine on the cardiovascular response to tracheal intubation
*F.A. Khan and R.S. Kamal* 394
Stellate ganglion block with bupivacaine. Minimum effective concentration of bupivacaine and the effect of added potassium
*P.A.J. Hardy* 398
Epidural diamorphine and bupivacaine in labour
*E.M.McGrady, D.K. Brownhill and A.G. Davis* 400

CASE REPORTS

Cardiovascular instability following bolus dose of etomidate
*E.M. McGrady and I.H. Wright* 404
Peri-operative management of severe thyrotoxicosis with esmolol
*H.R. Vijayakumar, W.O. Thomas and J.J. Ferrara* 406
Hypertrophic obstructive cardiomyopathy in combination with a prolapsing mitral valve. Anaesthesia for surgical correction with propofol
*M.D. Bell and C.S. Goodchild* 409

APPARATUS

The oesophageal detector device. A prospective trial on 100 patients
*K.N. Williams and J.F. Nunn* 412
Fluid flow through dural puncture sites. An *in vitro* comparison of needle point types
*R.H. Cruickshank and J.M. Hopkinson* 415
The pneuPAC ventilator with new patient valve and air compressors
*G.R. Park, A.R. Manara, A.R. Bodenham and C.J. Moss* 419
A modified expiratory valve for teaching
*A.J. Sansome and R. Bacon* 425

SPECIAL ARTICLE

Intensive care in the United Kingdom: report from the King's Fund panel 428

FORUM

Possible decrease in mortality associated with anaesthesia. A comparison of two time periods in Massachusetts, USA
*G.L. Zeitlin* 432
Spinal anaesthesia in infants born prematurely
*T.M. Gallagher and P.M. Crean* 434
Daycase anaesthesia and anxiety. A study of anxiety profiles amongst patients attending a Day Bed Unit
*J.W. Mackenzie* 437

SPECIAL ARTICLE

Report of a meeting of the International Committee for Prevention of Anesthesia Mortality and Morbidity
*J.B. Cooper* 441

CORRESPONDENCE 444

BOOK REVIEWS 452

ANAESTHETIC LITERATURE 454

HAZARD NOTICE 459

STOP PRESS 459

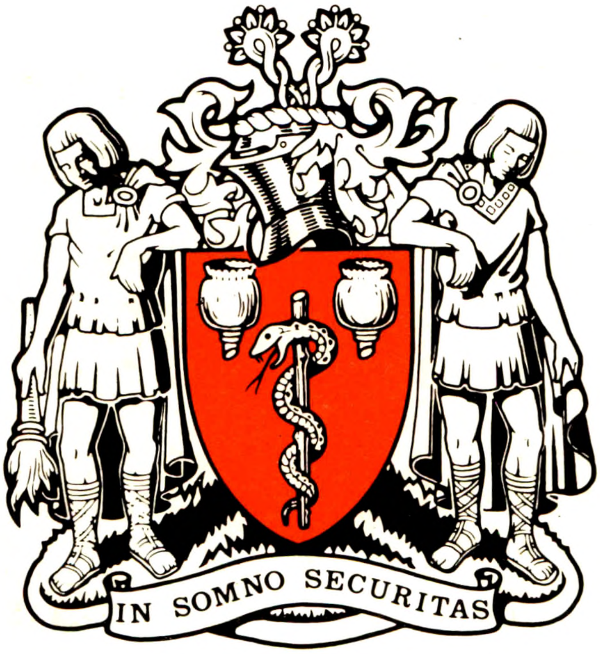
Typeset by Richard Clay Ltd, Bungay, Suffolk
Printed by The Whitefriars Press Ltd, member of BPCC Ltd, Tonbridge, Kent

5.12.90

# Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Volume 44 Number 6 June 1989

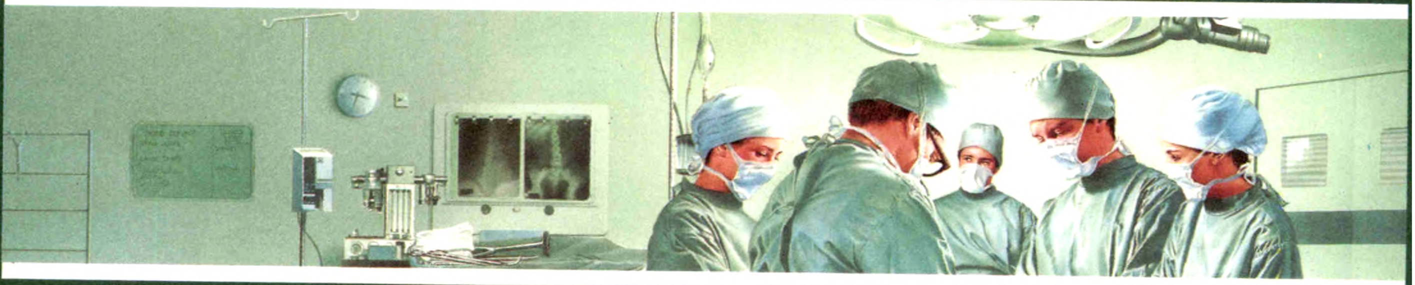


The Association of Anaesthetists of Great Britain and Ireland
*Patron*: HRH The Princess Margaret, Countess of Snowdon

Published for the Association by
Academic Press Grune & Stratton
London San Diego New York Boston
Sydney Tokyo Toronto

ISSN 0003-2409

# ANAESTHESIA HAS COME A LONG WAY...



# ...SO HAS REVERSAL

In recent years, many advances have been made in the field of anaesthesia, including reversal of residual neuromuscular blockade.

A. H. Robins has been a major contributor to this area with Robinul.

As an anticholinergic agent Robinul provides significant advantages over atropine: less initial tachycardia[1], better protection against the peripheral muscarinic effects of neostigmine[1], and a better quality of recovery[2].

At reversal, when administered simultaneously with neostigmine, Robinul is associated with greater cardiostability than separate injections[3].

ROBINUL – NEOSTIGMINE injection contains standard doses of Robinul and neostigmine in a 1ml ampoule, provides dependable and convenient reversal of residual neuromuscular blockade, and contributes further towards improvements in anaesthesia.

ROBINUL®
GLYCOPYRROLATE
NEOSTIGMINE
NEOSTIGMINE METHYLSULPHATE

POST op CARE

A·H·ROBINS

**PRESCRIBING INFORMATION** **Ingredients:** Each 1ml contains: Glycopyrrolate USP 500 micrograms (0.5mg) Neostigmine Methylsulphate BP 2500 micrograms (2.5mg). **Indication:** Reversal of residual non-depolarising (competitive) neuromuscular block. **Dosage and Administration:** Intravenous injection. Adults and Older Patients: 1-2ml (2500 micrograms neostigmine methylsulphate/500 micrograms glycopyrrolate to 5000 micrograms neostigmine methylsulphate/1000 micrograms glycopyrrolate) over a period of 10-30 seconds. Alternatively 0.02ml/kg (50 micrograms neostigmine methylsulphate/10 micrograms glycopyrrolate per kg body weight) over a period of 10-30 seconds. Children: 0.02ml/kg (50 micrograms neostigmine methylsulphate/10 micrograms glycopyrrolate per kg body weight) over a period of 10-30 seconds. These doses may be repeated if adequate reversal is not achieved. Total doses in excess of 2ml are not recommended. **Contra-indications:** Hypersensitivity to ingredients. Mechanical obstruction of gastrointestinal or urinary tracts. Concomitant administration of suxamethonium. **Side Effects:** Neostigmine induced (muscarinic) side effects – bradycardia, increased oropharyngeal secretions, cardiac dysrhythmias, bronchospasm, increased gastrointestinal activity etc. Glycopyrrolate induced side effects – dry mouth, difficulty in micturition, cardiac dysrhythmias, disturbances of visual accommodation, inhibition of sweating. **Precautions:** Use with caution in patients with bronchospasm, severe bradycardia, fever, glaucoma, coronary artery disease, congestive heart failure, cardiac dysrhythmias, hypertension, thyrotoxicosis, epilepsy or Parkinsonism. Use with caution in patients with intestinal anastomoses. Safety in pregnancy/lactation has not been established. **Basic NHS price** £10.37 (10 x 1ml ampoules). **Legal Category** POM **Package Quantities** Packs of 10 ampoules. **Further Information**

# Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editor J. N. LUNN
Associate Editor M. MORGAN
Assistant Editors R. GREENBAUM, A. R. AITKENHEAD, D. E. F. NEWTON
Editor of *Anaesthesia News* J. N. HORTON
*Editorial Board*
Chairman The President of the Association M. M. BURROWS
Members C. F. SCURR, P. J. F. BASKETT, J. EDMONDS-SEAL and a representative of the Junior Anaesthetists' Group
*Ex officio*
The Honorary Treasurer of the Association W. R. MACRAE
The Honorary Secretary of the Association W. L. M. BAIRD
The Immediate Past Honorary Secretary of the Association P. MORRIS

*Sub-editors of special sections*
L. KAUFMAN Anaesthetic literature
J. R. DAVIES Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

*Address for literary contributions* Dr J. N. Lunn, The Editor, *Anaesthesia*,
Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff
CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.

Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. A written statement of this acceptance may be requested by the Editor.

ANAESTHESIA: ISSN 0003–2409. Volume 44 1989, published monthly by Academic Press at 24–28 Oval Road, London NW1 7DX, UK, for the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
**All advertising** enquiries should be addressed to the Advertising Department, Anaesthesia, Harcourt Brace Jovanovich, 2nd Floor, 24–28 Oval Road, London NW1 7DX (Tel: 01-267 4466; Telex: 25775 ACPRES G; Fax: 01-482 2293).
Annual subscription price including postage: £98 UK and US $198 overseas. Subscription orders should be sent to Academic Press Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01–300 3322). Send notices of changes of address to the publisher at least 6–8 weeks in advance, including both old and new address.
Second class postage rate paid at Jamaica, NY 11431, USA.
Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmomont, NY 11003, USA.
USA POSTMASTERS: send change of addresses to ANAESTHESIA, c/o Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
Printed in UK.

© 1989 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the USA. This consent is given on the condition, within the USA, that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, USA for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the USA.

# Athena

## Using Technology to Meet the Demands of the Future.

Already installed in UK hospitals, Athena is proving its total flexibility in patient monitoring. Designed to keep pace with advances in technology, Athena is a fully modular system so that new parameter modules, program enhancements or more powerful components can easily be integrated as necessary.

Athena will collect, handle and present up to 16 physiological parameters on its high resolution 12″ monitor, from ECG and respiration through to cardiac out-put, endital C02 and oxygen saturation.

Central monitoring of up to 24 connected bedside scopes, and bed to bed communication are also available throughout the system, providing simple to operate, flexible, yet very sophisticated patient monitoring.

S&W

**S&W Vickers**

**S&W Vickers Ltd, Ruxley Corner, Sidcup, Kent DA14 5BL**
Telephone: 01-309 0433 Telex: 896328 Fax: 01-309 0919

**Sir Geoffrey Stephen William Organe**

*Anaesthesia*, 1989, Volume 44, pages 461–462

# Editorial

## Sir Geoffrey Stephen William Organe, MA, MRCS, LRCP, MB, BChir, MD, FFARCS, FFRACS(Hon), FRCS, FFARCS(Hon), DA

### 25 December 1908–7 January 1989

*Let us now praise Famous men, and our fathers that begat us.*
*Ecclesiasticus* 44, 1.

Geoffrey Stephen William Organe was born in Madras, on Christmas Day 1908, where his father the Rev. William Hartland Organe was a Congregationalist Minister. He was educated at Taunton School, contemporary with J. Alfred Lee, another renowned teacher of anaesthesia. He then proceeded to Christ's College Cambridge, where he was an outstanding athlete, and was one of the first high jumpers to use the Western roll.

His further medical education was at Westminster Hospital Medical School, his Alma Mater. A member of the Achilles Club, he was secretary, then captain, and later President of the United Hospitals Athletic Club. He was the first Consultant I met when, as a new boy in 1946, I was secretary of the Athletic Club and had to arrange the Sports Day, to which almost everyone came. Geoff, the President, took off his blazer, and in long flannels won the high jump yet again. Having represented the Hospital at most sports, he was regularly to be seen on the touchline, urging on the rugger team, even long after he retired.

He qualified MRCS LRCP in 1933. He went, after house jobs at Westminster, into General Practice, with Patrick Shackleton, who also later achieved distinction in anaesthesia as Professor at Southampton University. But general practice did not stretch him enough.

He became house anaesthetist at the Royal Berkshire Hospital and in 1937 took the Diploma in Anaesthesia. Not knowing the standard required, he claimed to have read and annotated all the available literature on anaesthesia, not impossible in those days! Magill took him back to Westminster Hospital as House Anaesthetist, and Diplomate in anaesthesia, probably better read than some of his recent examiners.

Later that year aged 28, he developed cancer of the colon and underwent a Paul–Mikulicz operation which today would be considered inadequate. Despite this, he survived over 50 years. The courage with which he endured the numerous operations and the long tedious months' recuperation was an inspiration to his friends. Magill gave him £100 and sent him on a holiday to recover. He and Peggy went by banana boat to the Canaries, along with a large box of sterile dressings. When they returned his fistula was almost healed.

He became the first Registrar anaesthetist at Westminster in 1938, and in the next year he was elected to the Honorary Consultant Staff. He was deemed unfit to serve in the Forces because of his cancer, and during the War he served in the Emergency Medical Service.

The War years underlined the courage which Geoffrey had exhibited in adversity. If an incendiary bomb fell on the hospital roof, he had to be there to see it. A characteristic memory is of the agile figure on the roof whose antics during the buzz bomb epidemic announced to less intrepid members of the hospital, the likelihood of imminent dissolution. He gave anaesthetics at all hours, and in all conditions. No-one ever saw him ruffled, or in a bad temper. He gave orders coolly in all circumstances, and established calm out of chaos. Westminster was a small hospital and medical school, and people who worked there were indeed members of an 'extended' family. Who had better fortune than to find in a young master as lucid an instructor and tolerantly companionable an elder 'brother' as Geoffrey Organe? He never aspired to artistry or dazzling technique, but a clear view of basic physiology and a reasoned simple explanation of what he did made him not only a wonderful teacher for beginners, but leaving little to chance, a good anaesthetist by the highest standards.

In the 1940s he suffered further adversity when he developed Dupuytren's contracture, which mainly affected his left hand, and had more than 25 operations, with an early amputation of his little finger. This was a most serious handicap for an anaesthetist using a laryngoscope before the advent of relaxants.

In the 1930s and 1940s, most anaesthetics were given by general practitioners, usually by inhalation of ether or chloroform. They were not all highly skilled anaesthetists, since they devoted only a small amount of their time to anaesthesia.

In 1938, he published a paper with R.J.B. Broad on nitrous oxide, oxygen and intermittent intravenous thiopentone for operations not requiring much muscle relaxation. They stated that 'for the patient the pleasantest forms of anaesthesia, from the point of view both of agreeable induction and of absence of undesirable after effects are provided by nitrous oxide and the short acting barbiturates'. This was the work which gained him his MD (Cantab.) in 1941.

He became secretary of the Medical Research Council Committee on Traumatic Shock from 1941 to 1947 which was of vital importance during the War.

He was involved in basic research on tubocurarine chloride to paralyse muscle as an adjunct to anaesthesia, with Stanley Rowbotham and Frederick Prescott; the latter was the conscious unanaesthetised subject on whom the effect of increasing doses were studied. He reported on the relaxant decamethonum iodide in anaesthesia in 1949, and the possibility of using pentamethonium iodide as an antidote was explored with W.D.M. Paton and Eleanor Zaimis. The hypotension which followed however, invalidated this use. It was later realised that this hypotensive action of pentamethonium might be used to spare the patient blood loss, and his colleagues, Scurr and Wyman initiated clinical trials. Independently, Enderby and Shackleton investigated a congener, hexamethonium, with similar properties.

In 1948, he was a founder member of the Faculty of Anaesthetists at the Royal College of Surgeons, starting

0003–2409/89/060461 + 02 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

as representative of the members, and as the youngest incumbent had the longest service of anyone on the Board. He was Clover lecturer and for many years an examiner for the DA and FFARCS and was Dean from 1958 to 1961.

He was a member of Council of the Section of Anaesthetics of the Royal Society of Medicine from 1953 to 1958, President of that Section, and later Secretary of the Society, and was elected Fellow in 1974.

He also held office in, and was President of, the Association of Anaesthetists of Great Britain and Ireland. In 1972 he was awarded the John Snow medal. Snow himself was the first to put anaesthesia on a scientific basis, and had been a student at Westminster Hospital, and had administered anaesthetics there.

In 1955 he became Secretary and Treasurer of the World Federation of Societies of Anaesthesiology. He visited the over 40 member countries worldwide as an Ambassador for British anaesthesia, educating and helping to raise standards. On one occasion he returned from overseas looking tanned and healthy. J.B. Wyman said, 'Dr Organe, will you please sign the Visitors' Book, while you are here'.

In 'Who's Who' he listed travel as his principal hobby. He visited, and taught for the British Council and the World Health Organisation in North and South America, Europe, including Czechoslovakia and USSR, Asia, Malaysia and Hong Kong, at a time when air travel was developing, and not without risk. He was adviser to the Department of Health, and Civilian Consultant to the Royal Navy. He was appointed Professor of Anaesthesia at Westminster Hospital Medical School in 1966. He was Knighted in 1968, when Britain was host to the 5th World Congress of Anaesthesia in London; only the fifth anaesthetist to be so honoured in 120 years of anaesthesia!

All his honours never changed him. He had a detached urbanity, a striving for impartiality and the right sensible and politic solution with avoidance of hasty decisions; he gave the feeling that emotion was rigorously suppressed. But he had a wry sense of humour. When Barrie Fairley, now Professor and Chairman of Anesthesia, at Stanford University, asked him for a testimonial when he was leaving Westminster to join the RAF Medical Service, he was given an excellent commendation as an anaesthetist but, to Barrie's consternation, at the end of his personal copy Geoff had had typed an addendum 'but he is a noisy eater of soup'—which was not true!

He had more than the average human share of physical affliction. He bore the suffering and incapacity involved with fortitude, so that his achievements were not thereby lessened. Thus he was a gifted anaesthetist with an unusually sympathetic approach to his patients. One never heard from him an uncharitable remark and he was slow to anger.

Life is a relay race. We all hope to hand on to posterity more than we have been given. Geoff was just such a relay runner. It is given to few men to be so gifted and achieve so much. To quote his namesake Geoffrey Chaucer, he was a 'Verray Parfait and Gentil Knyght'.

He is survived by his charming wife Peggy, his son Michael, and his daughters Janet and Sally and grandchildren.

*Ave, atque vale pater familias!*

*The Middlesex Hospital,*
*London W1N 8AA*

W.K. PALLISTER

## Editorial notices

### Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Manuscripts must be submitted in accordance with the internationally recognized *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979; I: 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

*Anaesthesia*, 1989, Volume 44, pages 463–466

# Crystalloid versus colloid for circulatory preload for epidural Caesarean section

A. M. MURRAY, M. MORGAN AND J. G. WHITWAM

## Summary

*Sixty mothers were randomly allocated to receive either 2 litres of crystalloid or 1 litre of colloid solution (hydroxyethyl starch) in order to preload the circulation prior to elective Caesarean section under epidural anaesthesia. There were no differences in the incidence of hypotension, degree of haemodilution, umbilical cord blood gas tensions or umbilical blood osmolalities between the two groups.*

**Key words**

*Anaesthesia, obstetric.*
*Anaesthetic techniques, regional*; epidural.

Epidural analgesia for elective and emergency Caesarean section is increasing in popularity and gradually replacing general anaesthesia. The problems of gastric aspiration and difficult tracheal intubation are virtually eliminated but, because a block to the height of $T_4$ must be attained,[1] are replaced by those of maintaining cardiovascular stability. Preloading the circulation is one of the mainstays in the prevention of hypotension, and use of a variety of volumes of crystalloid and colloid combinations has been described.[2–14] Despite this, a significant incidence of hypotension which necessitates the use of a vasopressor is still reported.[2,3] Different definitions of hypotension make comparisons of the relative merits of the various regimens difficult.

The usual practice in this department has been to use a 1 litre colloid circulatory preload, although no formal evaluation of its efficacy had ever been undertaken. It was therefore decided to compare our normal practice with a circulatory preload of 2 litres of crystalloid solution which is reported to be effective in the prevention of hypotension during Caesarean section under epidural anaesthesia.[5]

## Methods

Sixty consenting mothers who presented for elective Caesarean section under epidural anaesthesia were included in the study, which was approved by the local ethics committee. Exclusion criteria were pregnancy-induced hypertension, intra-uterine growth retardation, multiple pregnancy, diabetes mellitus, a coagulopathy or renal impairment. Oral ranitidine 150 mg was given the night before and again the morning of surgery. The mothers walked to the operating theatre where they received 0.3 M molar sodium citrate solution 30 ml.

Arterial blood pressure was recorded with an automatic device (Datascope) and the CM5 configuration of the ECG continuously displayed. An intravenous catheter was inserted in a peripheral vein and the mothers randomly allocated into two groups; one received 1 litre of compound sodium lactate (Hartmann's) solution over a 10-minute period before the epidural test dose, followed by a further litre given while the definitive dose of local anaesthetic took effect; the other group received hydroxyethyl starch (Hetastarch); the corresponding volumes were 500 ml on each occasion.

An epidural catheter was inserted 2–3 cm at the second or third lumbar interspace with the mother in the left lateral position. A further 20 ml of 0.5% plain bupivacaine was given through the epidural catheter after an uneventful test dose of 0.5% bupivacaine 3 ml with 1:200 000 adrenaline. Five minutes after the full dose, the mother was turned to the right lateral position and 15 minutes later the height of the block assessed using an ethyl chloride spray. If the height of the block was at $T_4$, preparations for surgery were begun, but if lower, increments of bupivacaine, 1.5 ml per unblocked segment below $T_4$, were given until the required height was attained. The mothers were positioned supine for surgery

---

A.M. Murray, FFARCS, Senior Registrar, M. Morgan, FFARCS, Reader in Anaesthetic Practice, J.G. Whitwam, PhD, FRCP, FFARCS, Professor, Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS.

Accepted 5 December 1988.

0003–2409/89/060463 + 04 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Details of patients ($n$ = 30 in each group).

| | Crystalloid | Colloid |
|---|---|---|
| Primiparae/multiparae | 7/23 | 9/21 |
| Age, years, mean (SD) | 30.4 (5.0) | 29.4 (5.8) |
| Weight, kg, mean (SD) | 74.6 (13.7) | 72.3 (13.2) |

**Table 2.** Distribution of decreases in systolic arterial blood pressure (SABP) in the two groups ($n$ = 30 each group).

| Decrease in SABP | Crystalloid | Colloid |
|---|---|---|
| < 10% | 2 (6.6%) | 4 (13.3%) |
| 11–20% | 16 (53%) | 7 (27.3%) |
| 21–30% | 6 (20%) | 13 (43.3%) |
| 31–40% | 4 (13.3%) | 6 (20.0%) |
| > 40% | 2 (6.6%) | 0 |
| Mean decrease (SD) | 21.85% (9.5) | 22.89% (9.9) |

**Table 3.** Systolic/diastolic arterial blood pressure (mmHg, mean, SD) 10 and 20 minutes after full dose of bupivacaine ($n$ = 30 in each group).

| | Crystalloid | Colloid |
|---|---|---|
| Baseline | 112.2 (11.2) 67.8 (9.97) | 113.8 (12.8) 71.3 (9.86) |
| 10 minutes | 108.3 (11.1) 66.8 (10.06) | 113.7 (13.5) 70.3 (9.2) |
| 20 minutes | 107.2 (12.3) 65.6 (9.35) | 108.6 (16.9) 63.7 (8.53) |

**Table 4.** Haematocrit (mean, SD) and umbilical arterial and venous acid base and blood gas values (mean, SD).

| | Crystalloid | Colloid |
|---|---|---|
| *Haematocrit* | | |
| preloading | 37% (4.25) | 37.5% (2.26) |
| after preloading | 31.9% (3.04) | 30.7% (3.25) |
| 24 hours | 34.4% (3.80) | 32.9% (3.41) |
| *Umbilical artery* | | |
| pH | 7.246 (0.076) | 7.223 (0.082) |
| $Po_2$ (kPa) | 1.78 (0.803) | 1.95 (0.81) |
| $Pco_2$ (kPa) | 6.86 (0.66) | 6.87 (0.98) |
| Base excess, mmol/litre | −7.54 (4.32) | −6.33 (4.28) |
| *Umbilical vein* | | |
| pH | 7.280 (0.073) | 7.305 (0.084) |
| $Po_2$ (kPa) | 3.18 (1.07) | 3.16 (1.06) |
| $Pco_2$ (kPa) | 5.59 (0.59) | 5.68 (0.88) |
| Base excess, mmol/litre | −6.04 (2.7) | −4.79 (2.2) |

with a wedge placed under the right buttock. Oxygen 4 litres/minute was administered via a Hudson mask until delivery, at which point syntocinon 10 units were given intravenously.

Arterial blood pressure and heart rate were measured every 2.5 minutes throughout the procedure. Hypotension was defined as a decrease in systolic arterial pressure of 20% or more from the baseline recording and was treated promptly with intravenous ephedrine 5–15 mg, repeated if necessary.

Maternal venous blood samples were taken for measurement of haematocrit before preloading, after preloading and 24 hours after operation. The haematocrit was measured by the anaesthetist using a microhaematocrit gauge; two samples were measured from each specimen. Umbilical arterial and venous blood was taken from a double clamped section of cord at delivery for measurement of gases, acid-base status and osmolality.

Statistical analysis of the results was performed using the Mann–Whitney *U* test, Student's *t*-test and the Chi-squared test.

## Results

Details of the patients are given in Table 1. There were no significant differences between the two groups with regard to age, weight or the distribution of parity.

The percentage decrease in systolic arterial pressure was calculated for each patient and the distribution of the results shown in Table 2. Twelve mothers (40%) who received compound sodium lactate solution had a decrease in systolic pressure greater than 20% from baseline values, compared to 19 (63%) of those given colloid. There was no significant difference between the two groups with regard to the overall distribution of hypotension nor the numbers that had a decrease greater than 20%. The lowest recorded systolic blood pressure in the crystalloid group was 69 mmHg and in those who received colloid 60 mmHg.

The arterial pressures 10 and 20 minutes after the full dose of bupivacaine are shown in Table 3. The differences between the groups was not significant. The time to the maximum decrease in blood pressure was 23.2 minutes (SD 10.8) in the crystalloid group and 22.7 minutes (SD 11.15) in the colloid.

The 12 patients in the crystalloid group whose arterial pressure decreased by more than 20% received between 12 and 40 mg of ephedrine (mean 22.1 mg). The corresponding amount of ephedrine given to the 19 patients in the colloid group was 6–60 mg (mean 23.1 mg).

The haematocrit and umbilical arterial and venous gases and acid base values are shown in Table 4. There was no statistically significant difference in these values between the groups, nor in the clinical condition of the neonates, which was assessed by the anaesthetist. The osmolality of the cord blood was a mean of 287.7 mosmol/kg (SD 7.15) in those who received crystalloid and 288.6 mosmol/kg (SD 3.9) in the colloid group. Fetal osmolality reflects maternal osmolality and the results of the study show that neither fluid regimen affected the osmolality.

Three mothers given crystalloid required extra bupivacaine after the initial 20-ml bolus, in amounts that varied between 4 and 10 ml, and similar amounts were given to four mothers who received colloid. The mean percentage decrease in blood pressure in the three mothers in the crystalloid group who required extra bupivacaine was 17%, compared with 16% in the four mothers in the colloid group who required extra bupivacaine.

## Discussion

Maternal hypotension has a number of undesirable effects. The incidence of nausea and vomiting under epidural anaesthesia is increased. Uterine tone is impaired, as is intervillous blood flow,[15,16] which in turn can lead to fetal bradycardia, acidosis and asphyxia. Ebner *et al.*[17] described fetal bradycardia occurring when maternal systolic arterial pressure was less than 80 mmHg for more than 4 minutes. These workers concluded that the duration of hypotension was probably more important than its degree in affecting the condition of the neonate. Others have concluded that a short period of hypotension (less than 2 minutes) did not affect the neurobehavioural performances of the newborn delivered by Caesarean section under spinal anaesthesia.[18]

Avoidance of aortocaval compression is mandatory; in a study which involved neither fluid preloading nor uterine

**Table 5.** Types of preloading and definition and incidences of hypotension reported in a sample of the literature. Hypotension refers to decrease in systolic arterial pressure.

| Authors | Preload | Definition of hypotension | Technique | Incidence of hypotension |
|---|---|---|---|---|
| Wilson *et al.*[2] | Crystalloid 1500 ml | <90 mmHg | Incremental epidural | |
| | | | plain | 36% |
| | | | with adrenaline | 45% |
| Laishley *et al.*[3] | Crystalloid 1000–2000 ml | < 100 mmHg or 20% decrease | Single shot epidural | 27.5% |
| Crawford *et al.*[4] | Crystalloid 1357–1852 ml | Decrease of 20 mmHg | Incremental epidural | 14.4% |
| Lewis *et al.*[5] | Crystalloid 2000 ml | Decrease of 20% | Incremental epidural | 7% |
| Ramanathan *et al.*[6] | Crystalloid 1200 ml | < 100 mmHg | Incremental epidural | 27% |
| | Crystalloid 700 ml + 5% albumin 700 ml | | | 22% |
| | Crystalloid 1000 ml + 25% albumin 200 ml | | | 22% |
| Hallworth *et al.*[7] | Crystalloid 1000 ml | <90 mmHg or decrease 30 mmHg | Incremental epidural | 45% |
| | Crystalloid 500 ml + colloid 500 ml | | | 5% |
| Thorburn and Moir[8] | Crystalloid 500 ml + colloid 500 ml | <90 mmHg | Incremental epidural | 16% |
| Mathru *et al.*[9] | Crystalloid 15 ml/kg | < 100 mmHg | Spinal | 33% |
| | Albumin 5% 15 ml/kg | Systolic or <85 mmHg mean | | 0 |
| Fox *et al.*[10] | Crystalloid 750–1000 ml | <90 mmHg | Single shot epidural | 45% |
| Downing *et al.*[11] | Crystalloid 500–1000 ml | >20 mmHg | Single shot epidural | 31.3% |
| Belfrage *et al.*[12] | Crystalloid 1000 ml | < 100 mmHg | Single shot epidural | 33% |
| Clark *et al.*[13] | Crystalloid 1000 ml | < 100 mmHg | Spinal | 52.8% |
| Wollman and Marx[14] | Crystalloid 1000 ml | >20% | Spinal | 0 |

displacement in mothers who had Caesarean section under spinal anaesthesia, the incidence of hypotension was 92%.[13] The addition of a fluid preload with or without uterine displacement reduced this figure in elective cases to 57% and 52% respectively. In emergency sections in labouring women, the incidence of hypotension was 46% using fluids only, but 14.7%, when uterine displacement was used as well.[13] A study which contained a group with no attempt to avoid aortocaval compression would not be justified nowadays. There would also appear to be little benefit from using an incremental epidural technique compared to a single shot (Table 5).

Preloading the maternal circulation to correct the relative hypovolaemia produced by the sympathetic blockade has become the prophylactic measure of choice in the prevention of hypotension, because of concern of the possible adverse effects of vasopressors on the neonate. But the best method of achieving this, and indeed its efficacy, is open to debate. Various combinations and volumes of crystalloid and (or) colloid solutions have been used, but none is entirely effective in the prevention of hypotension (Table 5). The situation is further complicated by the different definitions of hypotension; some take a decrease in arterial pressure below 100 mmHg, but in some mothers this is near their normal arterial pressure, while others use a fall of 20 or 30 mmHg. We have taken a decrease of 20% from baseline values, at which levels efforts were made to restore the pressure before the falls became excessive. A significant proportion of mothers in both groups were deemed hypotensive at this level, whereas if a decrease of 30% were regarded as critical, then only 20% of mothers in each group would be hypotensive.

Hydroxyethyl starch was used in this study as the colloid, which does not appear to have been used previously in obstetric practice. The volume of one litre is similar to the volume of albumin used by Mathru *et al.*[9] who reported a zero incidence of hypotension.

Hydroxyethyl starch is a 6% solution in normal saline. The mean osmotically active particle weight is 70 000, which is similar to albumin. It comprises a heterogenous group of molecules that range in molecular weight from under 10 000 to over 1 000 000. The smaller molecules are rapidly eliminated by glomerular filtration and 40% of the starch is excreted within 24 hours. The large polymers are hydrolysed by plasma α-amylase and are cleared once their size falls below the renal threshold. About 90% is eliminated from the body with a plasma half-life of 17 days, while the remainder is eliminated with a half-life of 48 days. About 30% of the dose infused leaves the vascular compartment and is taken up by the reticulo-endothelial system, and is claimed to have no adverse effect.

Theoretically, colloid solutions are the more logical choice to preload the circulation since they remain in it for a longer time, depending on their physical properties. About 75% of any crystalloid given diffuses into the interstitial space and about 2.5–3.0 times the volume of crystalloid is needed compared to colloid to achieve the same degree of expansion of the plasma volume. Immediately after preloading in the present study, there was no significant difference in the degree of haemodilution as judged by the haematocrit. The haematocrit was lower in the colloid group at 24 hours, but the difference was again not significant.

Neither colloid nor crystalloid solutions are without problems. The former may be associated with allergic reactions, although the incidence of severe events after hydroxyethyl starch is very low.[19] Problems with clotting were not found after 500–1500 ml of hydroxyethyl starch.[20] MacLennan *et al.*[21] found some mothers to have significantly increased lung water during the puerperium and these may be more susceptible to the effects of increased fluid loads, particularly in combination with other precipitating factors such as use of ergometrine or $\beta_2$-sympathomimetics. Excess crystalloids may produce pulmonary and peripheral oedema whilst having little effect on plasma volume. None of the patients studied showed any sign of these side effects.

A significant proportion of mothers require a vasopressor to treat hypotension despite a fluid preload, and the drug of choice has been shown to be ephedrine.[22] Used prophylactically, however, it is largely ineffective.[23,24] In over 1000 mothers given ephedrine 50 mg intramuscularly before Caesarean section under spinal anaesthesia, 46% had decreases in arterial pressure greater than 20%.[23] These workers found methoxamine to be more effective as a prophylactic, but at that time its effect on uterine blood flow had not been demonstrated.[22] Rolbin *et al.*[24] found no difference in the incidence of hypotension after prophylactic use of intramuscular ephedrine 25 mg, 50 mg or placebo in mothers who had also been acutely hydrated with one litre of crystalloid solution. They found that the 50-mg dose was associated with persistent hypertension in a number of mothers and also a decrease in umbilical pH. They did not recommend the use of prophylactic vasopressors. The most favourable results for mothers and fetus would appear to be achieved by an intravenous infusion of ephedrine[25] or intermittent boluses administered promptly.[26]

Elastic bandages applied to the legs have been shown to reduce significantly the occurrence of hypotension during epidural Caesarean section in mothers who had received 15 ml/kg compound sodium lactate solution.[27] Perhaps more widespread use of this simple method would reduce the use of vasopressors.

The results of the study reported here confirm the findings of others that preloading the circulation is an unreliable method of preventing hypotension during Caesarean section under epidural anaesthesia and that use of colloid rather than crystalloid solutions confers no advantage.

## References

1. Craft JB Jr, Roizen MF, Dao SD, Edwards M, Gilman R. A comparison of $T_4$ and $T_7$ dermatomal levels of analgesia for Caesarean section using the lumbar epidural technique. *Canadian Anaesthetists Society Journal 1982;* **29:** 264–9.
2. Wilson CM, Moore J, Ghaly RG, Flynn R, McClean E, Dundee JW. Plasma concentrations of bupivacaine during extradural anaesthesia for Caesarean section. The effect of adrenaline. *Anaesthesia* 1988; **43:** 12–5.
3. Laishley RS, Morgan BM. A single dose epidural technique for Caesarean section. A comparison between 0.5% bupivacaine plain and 0.5% bupivacaine with adrenaline. *Anaesthesia* 1988; **43:** 100–3.
4. Crawford JS, Davies P, Lewis M. Some aspects of epidural block provided for elective Caesarean section. *Anaesthesia* 1986; **41:** 1039–46.
5. Lewis M, Thomas P, Wilkes RG. Hypotension during epidural analgesia for Caesarean section. Arterial and central venous pressure changes after acute intravenous loading with two litres of Hartmann's solution. *Anaesthesia* 1983; **38:** 250–3.
6. Ramanathan S, Masih A, Rock I, Chalon J, Turndorf H. Maternal and fetal effects of prophylactic hydration with crystalloids or colloids before epidural anaesthesia. *Anesthesia and Analgesia* 1983; **62:** 673–8.
7. Hallworth D, Jellicoe JA, Wilkes RG. Hypotension during epidural anaesthesia for Caesarean section. A comparison of intravenous loading with crystalloid and colloid solutions. *Anaesthesia* 1982; **37:** 53–6.
8. Thorburn J, Moir DD. Epidural analgesia for elective Caesarean section. Technique and its assessment. *Anaesthesia* 1980; **35:** 3–6.
9. Mathru M, Rao TLK, Kartha RK, Shanmugham M, Jacobs KH. Intravenous albumin administration for prevention of spinal hypotension during Caesarean section. *Anesthesia and Analgesia* 1980; **59:** 655–8.
10. Fox GS, Smith JB, Namba Y, Johnson RC. Anesthesia for caesarean section: further studies. *American Journal of Obstetrics and Gynecology* 1979: **133:** 15–9.
11. Downing JW, Houlton PC, Barclay A. Extradural analgesia for Caesarean section: a comparison with general anaesthesia. *British Journal of Anaesthesia* 1979; **51:** 367–73.
12. Belfrage P, Irestedt L, Raabe N, Arner S. General anaesthesia or lumbar epidural block for Caesarean section? Effects on the foetal heart rate. *Acta Anaesthesiologica Scandinavica* 1977; **21:** 67–70.
13. Clark RB, Thompson DS, Thompson CH. Prevention of spinal hypotension associated with Cesarean section. *Anesthesiology* 1976; **45:** 670–4.
14. Wollman SB, Marx GF. Acute hydration for prevention of hypotension of spinal anesthesia in parturients. *Anesthesiology* 1968; **29:** 374–80.
15. Greiss FC Jr. Pressure-flow relationship in the gravid uterine vascular bed. *American Journal of Obstetrics and Gynecology* 1966; **96:** 41–7.
16. Jouppila R, Jouppila P, Kuikka J, Hollmen A. Placental blood flow during Caesarean section under lumbar extradural analgesia. *British Journal of Anaesthesia* 1978; **50:** 275–9.
17. Ebner H, Barcohana J, Bartoshuk AK. Influence of postspinal hypotension on the fetal electrocardiogram. *American Journal of Obstetrics and Gynecology* 1960; **80:** 569–72.
18. Corke BC, Datta S, Ostheimer GW, Weiss JB, Alper MH. Spinal anaesthesia for Caesarean section. The effect of hypotension on neonatal outcome. *Anaesthesia* 1982; **37:** 658–62.
19. Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet* 1977; **1:** 466–9.
20. Macintyre E, Mackie IJ, Ho D, Tinker J, Buffer C, Machin SJ. The haemostatic effects of hydroxyethyl starch (HES) used as a volume expander. *Intensive Care Medicine* 1985; **11:** 300–3.
21. Maclennan FM, Macdonald AF, Campbell DM. Lung water during the puerperium. *Anaesthesia* 1987; **42:** 141–7.
22. Ralston DH, Shnider SM, deLorimier AA. Effects of equipotent ephedrine, metaraminol, mephentermine and methoxamine on uterine blood flow in the pregnant ewe. *Anesthesiology* 1974; **40:** 354–70.
23. Moya F, Smith B. Spinal anesthesia for Caesarean section. Clinical and biochemical studies of effects on material physiology. *Journal of the American Medical Association* 1962; **179:** 609–14.
24. Rolbin SH, Cole AFD, Hew EM, Pollard A, Virgint S. Prophylactic intramuscular ephedrine before epidural anaesthesia for Caesarean section: efficacy and actions on the foetus and newborn. *Canadian Anaesthetists' Society Journal* 1982; **29:** 148–53.
25. Kang YG, Abouleish E, Caritis S. Prophylactic ephedrine infusion during C-section under spinal analgesia. *Anesthesiology* 1980; **53:** S301.
26. Datta S, Alper MH, Ostheimer GW, Weiss JB. Method of ephedrine administration and nausea and hypotension during spinal anesthesia for Cesarean section. *Anesthesiology* 1982; **56:** 68–70.
27. Gibbs CP, Werba JV, Banner TE, James CF, Hill CR. Epidural anesthesia: leg wrapping prevents hypotension. *Anesthesiology* 1983; **59:** A405.

*Anaesthesia*, 1989, Volume 44, pages 467–470

# Alkalinisation of bupivacaine for sciatic nerve blockade

D. M. COVENTRY AND J. G. TODD

**Summary**

*This double-blind study investigates the effect of pH adjustment of bupivacaine 0.5% with adrenaline 1:200 000, on block latency, duration of analgesia and systemic absorption of local anaesthetic after sciatic nerve blockade. Twenty-four adult patients were randomly allocated into one of two groups: Group A ($n = 12$) received bupivacaine with adrenaline 1:200 000 (pH 3.9) 2 mg/kg, while Group B ($n = 12$) received alkalinised bupivacaine with adrenaline 1:200 000 (pH 6.4) 2 mg/kg. Increasing the pH of the local anaesthetic solution significantly reduced block latency from 25 minutes in Group A to 12.5 minutes in Group B ($p < 0.001$) and prolonged the duration of useful analgesia from 14.1 hours to 18.3 hours ($p < 0.001$). There was no significant difference in plasma bupivacaine levels between the two groups. The results indicate that alkalinisation of bupivacaine reduces time to onset and prolongs the duration of useful analgesia when used for sciatic nerve blockade, without significantly increasing systemic absorption.*

**Key words**

*Anaesthetic techniques, regional*; sciatic nerve block.
*Anaesthetics, local*; bupivacaine.

Sciatic nerve blockade is a useful technique for providing intra-operative and postoperative analgesia for many operative procedures on the foot and lower limb. It is our practice to use bupivacaine for this purpose since it has a long duration of action in comparison to other agents currently available. The main disadvantage is its prolonged latency before satisfactory blockade is achieved.[1]

Local anaesthetic agents are weak bases prepared commercially as acidic salts to aid solubility and stability in solution. It has been demonstrated that the charged cationic molecule is required for conduction blockade while the uncharged base is necessary for adequate tissue penetration.[2–5] The proportion of each will depend on the pKa of the agent and the ultimate pH of the solution. By raising the pH of the local anaesthetic solution nearer to the physiological range, the fraction of uncharged base available for tissue penetration will be increased. Recent studies have shown that latency and duration of action of both lignocaine and bupivacaine can be favourably altered by this method.[6–9]

The purpose of this present study was to assess whether alkalinisation of bupivacaine produced any effect on the latency or duration of action of sciatic nerve blockade and to examine whether the systemic absorption of local anaesthetic is altered with the modified solution.

## Methods

Twenty-four adult patients who presented for elective foot surgery were studied. Those with known allergy to any agent involved were not included as were those with any neurological or neuromuscular disease including low back pain and sciatica. The study was approved by the local Research and Ethics Committee and formal informed consent obtained. All patients were premedicated with temazepam 20–30 mg orally, 1–2 hours before operation. The patients were randomly allocated into one of two groups. Group A received sciatic nerve block with bupivacaine 0.5% with adrenaline 1:200 000 (pH 3.9) in a dose of 2 mg/kg, while Group B received the same dose of the alkalinised solution (pH 6.4), prepared immediately before use with the addition of 0.1 mM (0.1 ml) of 8.4% sodium bicarbonate to each 10 ml of bupivacaine 0.5% with adrenaline 1:200 000.

On arrival in the anaesthetic room pulse rate and arterial blood pressure were checked and a 14-gauge cannula inserted into a large antecubital fossa vein to allow blood sampling for total plasma bupivacaine levels. Continuous temperature measurements were made from the dorsum of each foot as an indication of the onset of sympathetic blockade. The temperature measurements were made with

---

D.M. Coventry, FFARCS, Senior Registrar, J.G. Todd, FFARCS, Consultant, Division of Anaesthesia, Western Infirmary, Dumbarton Road, Glasgow G11 6NT.

Accepted 23 November 1988.

0003–2409/89/060467 + 04 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Patient data. Values expressed as mean (SD).

| | Group A<br>(plain bupivacaine)<br>($n$ = 12) | Group B<br>(alkalinised bupivacaine)<br>($n$ = 12) |
|---|---|---|
| Female | 10 | 10 |
| Male | 2 | 2 |
| Age, years | 54 (13) | 52 (16) |
| Weight, kg | 65 (11) | 59 (11) |

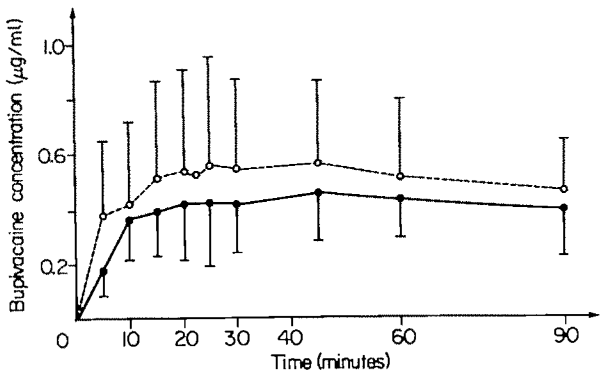


**Fig. 1.** Plasma bupivacaine levels, mean (SD) when using bupivacaine with adrenaline (●——●) or alkalinised bupivacaine with adrenaline (○——○).

an Ellab temperature monitor (DU 3s) connected to two thermocouples (Ellab AK20) and recorded continuously with a Curken two-channel potentiometric recorder.

Sciatic nerve blockade was performed by the posterior approach[10] using a 120-mm, 21-gauge insulated short bevelled needle and Stimuplex peripheral nerve stimulator (Braun Medical). The needle was advanced until plantar flexion of the foot was obtained with a current of 0.5 mA at 1 Hz and, after careful aspiration, the needle position was confirmed by the abolition of muscle twitches following a 2-ml test dose of the appropriate solution. The remainder of the solution was injected over a 2-minute period after confirmation of position. All blocks were performed by the same investigator (D.M.C.) and both patient and investigator were unaware of the solution used. Time to onset of sensory blockade was assessed at 2-minute intervals and defined as the time from completion of injection until loss of pinprick sensation with a short bevelled 25-gauge needle in both dorsal and plantar aspects of the foot. Temperature increase in the blocked limb was used to indicate the onset of sympathetic blockade. Complete or partial motor blockade was assessed by the ability of the patient to move his or her toes.

Ten-millilitre heparinised samples were taken at 5, 10, 15, 20, 25, 30, 45, 60 and 90 minutes after a baseline sample of 10 ml of venous blood. The samples were centrifuged and the plasma frozen until analysed for bupivacaine using high performance liquid chromatography. The extraction procedure was as described elsewhere.[11,12] Analysis was made in the following manner: the system used an Altex 110A Isocratic HPLC pump; the column was 15 cm × 4.6 mm, 5 μm ultrasphere ODS; the mobile phase consisted of a 65% Sorensons Phosphate Buffer (pH 6.50)/35%; acetonitrile at a flow rate of 2.0 ml/minute; ultraviolet detection at wavelength of 205 nm. The limit of detection was 0.020 μg/ml and coefficient of variation less than 5%.

General anaesthesia was induced with propofol and maintained with enflurane in nitrous oxide and oxygen with the patient breathing spontaneously through a Magill system by facemask, after satisfactory assessment of the regional blockade. This was necessary to cover tourniquet discomfort and for the personal preference of some patients. No systemic analgesics were administered in the peri-operative period and any complaint of discomfort on awakening was considered a block failure. The time to first analgesic requirement was used as an indicator of the duration of useful postoperative pain relief. Patients were prescribed morphine 10 mg intramuscularly or dextropopoxyphene 65 mg and paracetamol 650 mg as Coproxamol, two tablets 4-hourly on demand.

Statistical analyses of the results were performed using the Mann–Whitney *U* test. A probability value $<0.05$ was considered statistically significant.

## Results

There were no differences in age, weight or nature of surgery between the two groups. The surgical procedures consisted largely of first metatarsal osteotomies with silastic implants or fusion. There were a larger number of females in the study but the two groups were considered comparable as shown in Table 1. There was one failed block in Group B.

The results for latency of sympathetic block, analgesia to pinprick and loss of touch sensation are summarised in Table 2. The latency for all these modalities was significantly reduced in the alkalinised group. There was a variable degree of motor weakness with all the successful blocks which was complete in three patients in Group A and four patients in Group B; this difference was not significant.

Duration of pain relief as assessed by time to first analgesic requirement (Table 3) was significantly prolonged in Group B patients ($p < 0.001$). Five patients in each group required opioid analgesia after block regression.

Total plasma bupivacaine levels were greater at all times in Group B, but this difference did not reach statistical significance.

## Discussion

Sciatic nerve block is a useful technique for providing analgesia within its distribution in the lower extremity. It can be used for most operative procedures on the foot, with an appropriately placed below-knee tourniquet or combined with a light general anaesthetic if a thigh tourniquet is preferred. In addition, it can be used in combination with lumbar plexus block[13,14] to provide complete analgesia of the lower extremity in situations where central neuronal blockade is either contraindicated or technically difficult.

One of the main advantages of peripheral blockade with bupivacaine is the long duration of action when compared to extradural or spinal analgesia. However, it does have the disadvantage in our experience of a prolonged latency which is reported to be in the region of 30–45 minutes.[1,10] Latency should not influence the decision to utilise a sciatic nerve block when considered the most appropriate anaesthetic technique, but in practice this appears to deter many anaesthetists, particularly when success is not

**Table 2.** Onset of nerve blockade, minutes. Values expressed as mean (range).

| | Group A (plain bupivacaine) ($n = 12$) | Group B (alkalinised bupivacaine) ($n = 11$) | p |
|---|---|---|---|
| Sympathetic block | 16.5 (10–24) | 7.5 (2–15) | <0.001 |
| Analgesia to pinprick | 25.0 (14–38) | 12.5 (4–20) | <0.001 |
| Touch* | 33.5 (22–45) | 22.5 (12–36) | <0.05 |

* Loss of touch sensation occurred in Group A ($n = 6$) and Group B ($n = 9$).

**Table 3.** Duration of useful analgesia, hours. Values expressed as mean (range).

| | Group A (plain bupivacaine) ($n = 12$) | Group B (alkalinised bupivacaine) ($n = 11$) | p |
|---|---|---|---|
| First analgesic requirement, hours | 14.1 (10.5–18.5) | 18.3 (14–24) | <0.001 |
| Complete analgesia at 15 hours | 3.0 | 10.0 | <0.01 |

guaranteed. Many attempts have been made to improve its onset characteristics with a variety of regional blocks. These have included the addition of dextran,[15] potassium,[16] carbonation,[17] increasing the concentration of the agent[18] and the alteration of solution temperature.[19,20] Mixing of rapidly acting and longer acting agents has been advocated to induce a nerve block with the best characteristics of each individual agent.[21] This technique, however, complicates estimation of potential toxic dosage and appears with chloroprocaine to confer characteristics that resemble the shorter acting agent rather than the bupivacaine.[6,22] It appears possible, however, to prolong duration further when the pH of the mixture is raised to that of the original bupivacaine solution.[6] Similarly, the addition of dextran solutions to reduce latency would seem to act by raising pH and therefore increasing tissue solubility.[15]

Recent studies have suggested that raising the pH of bupivacaine even nearer to the physiological range will result in a higher proportion of uncharged base and therefore increased tissue solubility, to allow a more rapid diffusion and penetration through the connective tissue nerve sheaths.[7–9] The sciatic nerve is the largest peripheral nerve in the body so it appears to be the most suitable for study. Latency and efficacy of clinical nerve block are largely dependent on accurate placement of the needle in relation to the nerve trunk, and it is therefore important that the technique is standardised as much as possible. This is best achieved with a peripheral nerve stimulator, which also has the advantage of avoiding the need to elicit paraesthesia, with the subsequent risk of neuronal damage, particularly if short-bevelled insulated needles are not used.[23–26]

Our results demonstrate that alkalinisation of bupivacaine produces a statistically and clinically significant reduction in block latency, as well as prolongation of useful postoperative analgesia. Plasma bupivacaine levels were well within the postulated safe limit of 4 μg/ml,[27] which indicates the slow systemic absorption from this site previously seen with bupivacaine and other agents.[28,29] This again emphasises the importance of the site of injection of local anaesthetic rather than a recommended 'safe dose' to be used for all regional blocks[30] and may have implications for carrying out combined sciatic and femoral blocks using bupivacaine.

## Acknowledgments

The authors thank Mr E. Anderson, Consultant Orthopaedic Surgeon for his cooperation in this study; Mr J. Smith of the University Department of Anaesthesia, Glasgow Royal Infirmary, for analysis of the samples and Mrs J. Scott for her assistance in preparing the manuscript.

## References

1. Thorburn J, Rogers KM. Orthopaedic surgery. In: Henderson JJ, Nimmo WS, eds. *Practical regional anaesthesia.* Oxford: Blackwell Scientific, 1983: 184–214.
2. Ritchie JM, Greengard P. On the active structure of local anaesthetics. *Journal of Pharmacology and Experimental Therapeutics* 1961; **133:** 241–5.
3. Ritchie JM, Ritchie B, Greengard P. The active structure of local anaesthetics. *Journal of Pharmacology and Experimental Therapeutics* 1965; **150:** 152–9.
4. Ritchie JM, Ritchie B, Greengard P. The effect of the nerve sheath on the action of local anaesthetics. *Journal of Pharmacology and Experimental Therapeutics* 1965; **150:** 160–4.
5. Wildsmith JAW. Peripheral nerve and local anaesthetic drugs. *British Journal of Anaesthesia* 1986; **58:** 692–700.
6. Galindo A, Witcher T. Mixtures of local anaesthetics: bupivacaine–chloroprocaine. *Anesthesia and Analgesia* 1980; **59:** 683–5.
7. DiFazio CA, Carron H, Grosslight KR, Moscicki JC, Bolding WR, Johns RA. Comparison of pH-adjusted lidocaine solutions for epidural anesthesia. *Anesthesia and Analgesia* 1986; **65:** 760–4.
8. McMorland GH, Douglas MJ, Jeffrey WK, Ross PLE, Axelson JE, Kim JHK, Gambling DR, Robertson K. Effect of pH-adjustment of bupivacaine on onset and duration of epidural analgesia in parturients. *Canadian Anaesthetists' Society Journal* 1986; **33:** 537–41.
9. Hilgier M. Alkalinisation of bupivacaine for brachial plexus block. *Regional Anesthesia* 1985; **8:** 59–61.
10. Lofstrom B, Englesson S. Nerve block in the region of the hip-joint. In: Eriksson E, ed. *Illustrated handbook in local anaesthesia*, 2nd edn. London: Lloyd-Luke, 1979: 101–10.
11. Tucker GT. Determination of bupivacaine (Marcain) and other anilide-type local anesthetics in human blood and plasma by gas chromatography. *Anesthesiology* 1970; **32:** 255–60.
12. Zylber-Katz E, Granit L, Levy M. Gas-liquid chromatographic determination of bupivacaine and lidocaine in plasma. *Clinical Chemistry* 1978; **24:** 1573–5.
13. Chayen D, Nathan H, Chayen M. The psoas compartment block. *Anesthesiology* 1976; **45:** 95–9.
14. Winnie AP, Ramamurthy S, Durrani Z. The inguinal paravascular technic of lumbar plexus anesthesia: the '3-in-1' block. *Anesthesia and Analgesia* 1973; **52:** 989–96.
15. Rosenblatt R. Dextran as a local anesthetic adjuvant; its history and current status. *Regional Anesthesia* 1981; **6:** 108–11.
16. Parris MR, Chambers WA. Effects of the addition of potassium to prilocaine or bupivacaine studies on brachial plexus blockade. *British Journal of Anaesthesia* 1986; **58:** 297–300.
17. Brown DR, Morison DH, Covino BG, Scott DB.

Comparison of carbonated bupivacaine and bupivacaine hydrochloride for extradural anaesthesia. *British Journal of Anaesthesia* 1980; **52:** 419–22.

18. Smith BE, Siggins D. Low volume, high concentration block of the sciatic nerve. *Anaesthesia* 1988; **43:** 8–11.
19. Mehta PM, Theriot E, Mehrotra D, Patel K, Kimball BG. A simple technique to make bupivacaine a rapid-acting epidural anesthetic. *Regional Anesthesia* 1987; **12:** 135–8.
20. Paul DL, Logan MR, Wildsmith JAW. The effects of injected solution temperature on intravenous regional anaesthesia. *Anaesthesia* 1988; **43:** 362–4.
21. Cunningham NL, Kaplan JA. A rapid-onset, long-acting regional anesthetic technique. *Anesthesiology* 1974; **41:** 509–11.
22. Kim JM, Goto H, Arakawa K. Duration of bupivacaine intradermal anesthesia when bupivacaine is mixed with chlorprocaine. *Anesthesia and Analgesia* 1979; **58:** 364–6.
23. Selander D, Dhuner KG, Lundborg G. Peripheral nerve injury due to injection needles used for regional anaesthesia. An experimental study of the acute effects of needle point trauma. *Acta Anaesthesiologica Scandinavica* 1977; **21:** 182–8.
24. Selander D, Edshage S, Wolff T. Paraesthesia or no paraesthesia? Nerve lesions after axillary blocks. *Acta Anaesthesiologica Scandinavica* 1979; **23:** 27–33.
25. Bashein G, Haschke RH, Ready LB. Electrical nerve location: numerical and electrophoretic comparison of insulated vs uninsulated needles. *Anesthesia and Analgesia* 1984; **63:** 919–24.
26. Ford DJ, Pither C, Raj PP. Comparison of insulated and uninsulated needles for locating peripheral nerves with a peripheral nerve stimulator. *Anesthesia and Analgesia* 1984; **63:** 925–8.
27. Jordfeldt L, Lofstrom B, Pernow B, Persson B, Wahren J, Widman B. The effect of local anaesthetics on the central circulation and respiration in man and dog. *Acta Anaesthesiologica Scandinavica* 1968; **12:** 153–69.
28. Tucker GT, Moore DC, Bridenbaugh PO, Bridenbaugh LD, Thompson GE. Systemic absorption of mepivacaine in commonly used regional block procedures. *Anesthesiology* 1972; **37:** 277–87.
29. Moore DC, Mather LE, Bridenbaugh LD, Balfour RI, Lysons DF, Horton WG. Arterial and venous plasma levels of bupivacaine following peripheral nerve blocks. *Anesthesia and Analgesia* 1976; **55:** 763–8.
30. Neill RD, Watson R. Plasma bupivacaine concentrations during combined regional and general anaesthesia for resection and reconstruction of head and neck carcinomata. *British Journal of Anaesthesia* 1984; **56:** 485–91.

*Anaesthesia*, 1989, Volume 44, pages 471–474

# Comparison of hyperbaric and plain bupivacaine with hyperbaric cinchocaine as spinal anaesthetic agents

F. L. ROBERTS, E. C. BROWN, R. DAVIS AND M. J. COUSINS

## Summary

*In a double-blind study, 90 patients (ASA 1 or 2) received spinal anaesthesia with 2 ml hyperbaric cinchocaine 0.5%, 4 ml hyperbaric bupivacaine 0.5% or 4 ml plain bupivacaine 0.5%. All injections were made in the left lateral position, and the patients turned supine immediately. Hyperbaric bupivacaine produced a significantly faster and a higher dermatomal level of bilateral complete sensory blockade than the other solutions ($p < 0.005$ for each). The duration of sensory blockade was significantly longer with plain bupivacaine than with either hyperbaric solution ($p < 0.0005$). The intensity of sensory blockade was significantly greater with both bupivacaine solutions than with hyperbaric cinchocaine ($p < 0.05$). Onset and intensity of motor blockade were similar with all agents, but motor blockade was of significantly shorter duration with hyperbaric bupivacaine than the other agents ($p < 0.0005$). Hyperbaric bupivacaine appears to be the best agent for rapid and intense sensory blockade of intermediate duration. Plain bupivacaine is more appropriate if a longer duration of action but a lower height of blockade are required, and has the advantage of less cardiovascular disturbance.*

## Key words

*Anaesthetic techniques, regional*; spinal.
*Anaesthetics, local*; cinchocaine, bupivacaine.

Variation among countries in the availability of agents for spinal anaesthesia is both perplexing and frustrating for the anaesthetist. Amethocaine (tetracaine), the most popular agent in the United States, is not widely available in Australia or the United Kingdom. Lignocaine, also used extensively in the United States, is not licensed for use in the United Kingdom. Cinchocaine, which was for many years the only agent available for spinal anaesthesia in Australia and the United Kingdom, has recently been withdrawn, although bupivacaine, in plain and hyperbaric preparations, is now available for spinal use. Several studies have compared bupivacaine with amethocaine[1–3] and lignocaine[4,5] for spinal use, but only one has compared plain and hyperbaric bupivacaine with hyperbaric cinchocaine,[6] and that study specifically excluded the elderly. Patients in this age group present frequently for surgery, notably urological and orthopaedic procedures, for which spinal anaesthesia is appropriate. It has been suggested that the response to spinal anaesthesia varies with age.[7–9]

This prospective study compared the use of hyperbaric and plain bupivacaine with hyperbaric cinchocaine in a population with no age restriction. In addition, larger numbers of patients were used than in the previous study[6] (30 instead of 10 in each group).

## Methods

Ninety patients, ASA grade 1 or 2, who presented for urological or lower body surface surgery, and in whom no contraindication to spinal anaesthesia existed, were studied. Informed consent was obtained from all patients, and the study was approved by the hospital ethics committee.

Each patient was premedicated with oral temazepam 10 or 20 mg, 1–2 hours pre-operatively. A 16-gauge intravenous cannula was inserted, and a small preload of compound sodium lactate solution given. A lumbar puncture was performed with the patient in the left lateral position, through the $L_{3/4}$ interspace, using a 25-gauge

---

F.L. Roberts,* FFARCS, Senior Registrar, E.C. Brown, FFARACS, Staff Specialist, R. Davis, FFARACS, Senior Specialist, Department of Anaesthesia and Intensive Care, Repatriation General Hospital, Daw Park, South Australia, Australia, 5041, M.J. Cousins, MD, FFARACS, FFARCS, Professor and Chairman, Department of Anaesthesia and Intensive Care, Flinders Medical Centre, Bedford Park, South Australia, Australia, 5042.

* Current address, to which correspondence should be sent: Department of Anaesthesia, Royal Devon and Exeter Hospital (Wonford), Barrack Road, Exeter, EX2 5DW, UK.

Accepted 30 November 1988.

0003–2409/89/060471 + 04 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Patient characteristics. Data are presented as mean (SD). HC, hyperbaric cinchocaine; HB, hyperbaric bupivacaine; PB, plain bupivacaine.

| | Group HC | Group HB | Group PB |
|---|---|---|---|
| Age, years | 68 (6) | 68 (5) | 69 (6) |
| Weight, kg | 75 (8) | 76 (11) | 72 (11) |
| Height, cm | 175 (5) | 176 (7) | 172 (8) |
| Duration of surgery, minutes | 35 (21) | 30 (18) | 32 (14) |

**Table 2.** Bilateral sensory blockade: time (minutes) to reach a height of $T_{12}$, maximum dermatomal height of blockade, time (minutes) to regression by three or more segments [data presented as mean (SD)], and number of patients in each group with $S_1$ blockade. HC, hyperbaric cinchocaine; HB, hyperbaric bupivacaine; PB, plain bupivacaine.

| | Group HC | Group HB | Group PB | p |
|---|---|---|---|---|
| Time to $T_{12}$ | 10.9 (4.7) | 7.3 (5.0) | 8.6 (5.8) | < 0.005* |
| Highest thoracic dermatome blocked | 10.1 (3.0) | 8.4 (3.2) | 11.3 (3.5) | < 0.005* |
| Time to three segment regression | 113 (40) | 95 (29) | 157 (70) | < 0.0005** |
| $S_1$ blockade | 18/30 | 27/30 | 24/30 | < 0.05*** |

* HB different from HC and PB.
** PB different from HB and HC.
*** HC different from HB and PB.

needle. Patients were allocated randomly to receive 2 ml of cinchocaine 0.5% in 6% dextrose (Group HC), 4 ml of bupivacaine 0.5% in 8% dextrose (Group HB) or 4 ml of plain bupivacaine 0.5% (Group PB). The injection was made over 15–20 seconds, without barbotage, and the patient turned supine immediately. An independent assessor (the same person throughout the study), who was unaware of the drug used, evaluated the block every 2 minutes until the maximal extent of sensory block had occurred. The sensory block was tested using loss of touch sensation to the blunt end of a standard hypodermic needle, and the cephalad and caudal extent of the block on both left and right sides was recorded. Motor block was assessed using the Bromage scale.[10]

The electrocardiogram (CM5 lead) was displayed continuously and the arterial pressure was recorded every 5 minutes by an automatic noninvasive device. Hypotension (systolic arterial pressure less than 100 mmHg) was treated with intravenous fluid and (or) incremental doses of ephedrine 3 mg intravenously, plus 30 mg intramuscularly if hypotension persisted. Bradycardia (heart rate less than 50 beats/minute) was treated with incremental doses of atropine 0.1 mg. Any additional requirements for anaesthesia during surgery were noted. Postoperative observations were continued every 15 minutes until complete regression of the block had occurred. Each patient was visited 48 hours postoperatively and any complications recorded.

Kruskal–Wallis analysis of variance was used to identify any overall variation among groups. Where significant variation occurred, the Mann–Whitney test was used to show which groups differed. The Chi-squared test was used to compare the frequency of $S_1$ blockade among groups. A probability of less than 0.05 was regarded as significant.

## Results

There were no significant differences among groups in respect of age, height, weight or duration of surgery (Table 1). The age range was from 54 to 81 years.

Details of sensory blockade are displayed in Table 2 and Figure 1. The time to onset of bilateral sensory blockade to a height of $T_{12}$ was significantly shorter in group HB than in groups HC and PB. The maximum height of bilateral sensory blockade was significantly greater in group HB than in groups HC and PB. Regression of sensory blockade by three or more dermatomal segments bilaterally took significantly longer to occur in group PB than in groups HC and HB. Bilateral sensory blockade of the $S_1$ dermatome occurred significantly more frequently in groups HB and PB than in group HC.

There were no significant differences in time to onset of complete bilateral motor blockade among the groups (Table 3). There were no differences in the frequency of complete bilateral motor blockade (27 patients in each group). The time to complete recovery from motor blockade was significantly shorter in group HB than in groups HC and PB.

The maximum decrease in systolic blood pressure was significantly lower in group PB than in groups HC and HB (Table 4). The ephedrine dosage used was significantly lower in group PB than in groups HC and HB. The decrease in heart rate was small in all groups, with no differences among groups. Only four patients required atropine.

One patient (Group PB) required a general anaesthetic because of an inadequate block. Two patients complained of postspinal headache, but neither required any treatment other than bed rest and simple analgesia.

## Discussion

We have compared the effects of spinal anaesthesia undertaken using the two agents currently available in Australia and the United Kingdom with those associated with the drug available previously. The dose of bupivacaine used (4 ml 0.5%) is at the upper end of the range reported previously for safe use,[7,11,12] and the cinchocaine dose (2 ml 0.5%) is in the same proportion to bupivacaine as that used in a previous comparison.[6] Loss of touch sensation (anaesthesia) was used rather than loss of pinprick sensation (analgesia) for assessment of sensory blockade, since we found it an easier endpoint for elderly patients to distinguish. Dermatomal level of surgical anaesthesia has been shown previously to be related consistently to level of analgesia, approximately 2–3 segments lower than the

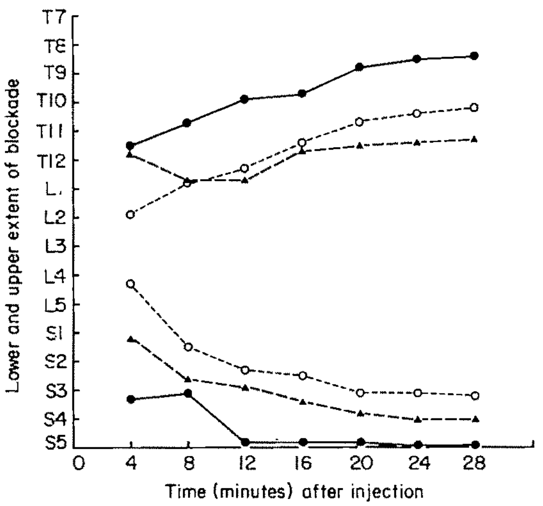


**Fig. 1.** Progression of bilateral sensory blockade. Data points represent mean values of upper and lower limits of block at each time point after injection of hyperbaric bupivacaine (HB), plain bupivacaine (PB) or hyperbaric cinchocaine (HC). ●——●, HB; ▲--▲, PB; O--O, HC.

**Table 3.** Onset and recovery times (minutes) for complete bilateral motor blockade. Data are presented as mean (SD). HC, hyperbaric cinchocaine; HB, hyperbaric bupivacaine; PB, plain bupivacaine.

| | Group HC | Group HB | Group PB | p |
|---|---|---|---|---|
| Onset | 9.6 (5.6) | 8.7 (4.1) | 10.8 (4.6) | NS |
| Recovery | 297 (33) | 216 (57) | 308 (20) | < 0.0005* |

* HB different from HC and PB.

**Table 4.** Maximum decreases in systolic arterial pressure (SAP, mmHg), heart rate (HR, beats/minute), and ephedrine dosage (mg). Data are presented as mean (SD). HC, hyperbaric cinchocaine; HB, hyperbaric bupivacaine; PB, plain bupivacaine.

| | Group HC | Group HB | Group PB | p |
|---|---|---|---|---|
| Maximum decrease in SAP | 39 (25) | 34 (18) | 15 (13) | < 0.0005* |
| Maximum decrease in HR | 3 (4) | 6 (8) | 4 (4) | NS |
| Ephedrine dosage | 13 (16) | 15 (13) | 3 (8) | < 0.0005* |

* PB different from HC and HB.

dermatomal level of analgesia.[6,13] The time taken to reach a height of $T_{12}$ was used to determine onset since it represented an adequate extent of blockade for most lower body surgery. The duration of blockade was assessed by measurement of time to regression by three or more dermatomal segments bilaterally. This, rather than regression to $T_{12}$, was selected for comparing the three groups, because they had different extents of blockade.

We have shown that hyperbaric bupivacaine produces the most rapid onset of sensory blockade of the drugs tested. This had not been shown conclusively before.[6] Additionally, hyperbaric bupivacaine produced the most extensive blockade; the mean height of blockade was $T_8$, compared to $T_{10}$ for hyperbaric cinchocaine and $T_{11}$ for plain bupivacaine. The difference in height of block between the hyperbaric and plain preparations of bupivacaine, when given in the lateral position (turning immediately supine), is similar to that reported for amethocaine.[14] The likely explanation is the gravitational spread of the hyperbaric solution into the thoracic hollow in the supine patient.

A higher block with plain bupivacaine can be obtained by injecting the drug with the patient seated,[15] although this is at the expense of a shorter duration of action. In the present study, the duration of block decreased as the height of the blockade increased. Removal of local anaesthetic from neural tissue in the subarachnoid space is by a combination of diffusion into the cerebrospinal fluid, vascular absorption into the vessels of the spinal cord and diffusion across the dura with subsequent vascular absorption from the epidural space.[16] A higher block presents a greater surface area for these processes, and therefore might be expected to lead to more rapid elimination of the drug.

Comparison of intensity of sensory blockade was made using complete bilateral blockade of $S_1$, the nerve root of greatest diameter and the most resistant to blockade.[17] We found both preparations of bupivacaine to produce blockade of $S_1$ more frequently than hyperbaric cinchocaine. Previous work had found hyperbaric bupivacaine to produce more effective spinal anaesthesia for Caesarean section than hyperbaric cinchocaine.[18] The frequency of $S_1$ blockade in all groups was far higher than that reported previously for epidural blockade with 2% lignocaine or 0.5% bupivacaine;[19] this suggests that spinal anaesthesia produces more intense sensory blockade than epidural anaesthesia.

The smallest haemodynamic changes occurred in the plain bupivacaine group, which also had the lowest height of blockade. This was reflected in a lesser requirement for ephedrine. The substantial doses of ephedrine used represent a policy in our department for early use of vasopressors to treat hypotension in elderly patients in preference to the infusion of large volumes of fluid. Previous work has failed to show a correlation between height of blockade and degree of hypotension.[12,13] In this study, however, an agent-specific effect was suggested by the greater cardiovascular stability seen with plain bupivacaine.

In conclusion, hyperbaric bupivacaine produced spinal anaesthesia of quicker onset, higher dermatomal level, greater intensity and similar duration of blockade compared with hyperbaric cinchocaine. Hyperbaric bupivacaine also has the benefits of thermostability and photostability, and appears to have many advantages over hyperbaric cinchocaine. Plain bupivacaine is an attractive agent for a lower level of blockade of greater duration, and greater cardiostability.

## Acknowledgments

We thank Mrs B. Lee, RN, for her meticulous testing throughout the study, and also Astra (Australia) Pharmaceuticals Pty Ltd for their support.

## References

1. Pflug AE, Aasheim GM, Beck HA. Spinal anesthesia: bupivacaine versus tetracaine. *Anesthesia and Analgesia* 1976; **55:** 489–92.
2. Moore DC. Spinal anesthesia: bupivacaine compared with tetracaine. *Anesthesia and Analgesia* 1980; **59:** 743–50.
3. Tattersall MP. Isobaric bupivacaine and hyperbaric amethocaine for spinal analgesia. A clinical comparison. *Anaesthesia* 1983; **38:** 115–9.
4. Millar JM, Jago RH, Fawcett DP. Spinal analgesia for transurethral prostatectomy. Comparison of plain bupivacaine and hyperbaric lignocaine. *British Journal of Anaesthesia* 1986; **58:** 862–7.
5. Ewart MC, Rubin AP. Subarachnoid block with hyperbaric lignocaine. A comparison with hyperbaric bupivacaine. *Anaesthesia* 1983; **42:** 1183–7.
6. Cummings GC, Bamber DB, Edstrom HH, Rubin AP. Subarachnoid blockade with bupivacaine. A comparison with cinchocaine. *British Journal of Anaesthesia* 1984; **56:** 573–9.
7. Cameron AE, Arnold RW, Ghoris MW, Jamieson V. Spinal anaesthesia using bupivacaine 0.5% plain. Variation in the extent of the block with patient age. *Anaesthesia* 1981; **36:** 318–22.
8. Pitkanen M, Haapaniemi L, Tuominen M, Rosenberg PH. Influence of age on spinal anaesthesia with isobaric 0.5% bupivacaine. *British Journal of Anaesthesia* 1984; **56:** 279–84.
9. Veering BT, Burm AGL, Spierdijk J. Spinal anaesthesia with hyperbaric bupivacaine. Effects of age on neural blockade and pharmacokinetics. *British Journal of Anaesthesia* 1988; **60:** 187–94.
10. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. *Acta Anaesthesiologica Scandinavica* 1965; **16** (Suppl.): 55–69.
11. Chambers WA, Littlewood DG, Edstrom HH, Scott DB. Spinal anaesthesia with hyperbaric bupivacaine: effects of concentration and volume administered. *British Journal of Anaesthesia* 1982; **54:** 75–80.
12. Sheskey MC, Rocco AG, Bizzarri-Schmid M, Francis DM, Edstrom H, Covino BG. A dose-response study of bupivacaine for spinal anesthesia. *Anesthesia and Analgesia* 1983; **62:** 931–5.
13. Chambers WA, Edstrom HH, Scott DB. Effect of baricity on spinal anaesthesia with bupivacaine. *British Journal of Anaesthesia* 1981; **53:** 279–82.
14. Brown DT, Wildsmith JAW, Covino BG, Scott DB. Effect of baricity on spinal anaesthesia with amethocaine. *British Journal of Anaesthesia* 1980; **52:** 589–96.
15. Tuominen M, Kalso E, Rosenberg PH. Effects of posture on the spread of spinal anaesthesia with isobaric 0.75% or 0.5% bupivacaine. *British Journal of Anaesthesia* 1982; **54:** 313–8.
16. Greene NM. Uptake and elimination of local anesthetics during spinal anesthesia. *Anesthesia and Analgesia* 1983; **62:** 1013–24.
17. Galindo A, Hernandez J, Benavides O, Ortegon-de-Munoz S, Bonica JJ. Quality of spinal extradural anaesthesia: the influence of spinal nerve root diameter. *British Journal of Anaesthesia* 1975; **47:** 41–7.
18. Michie AR, Freeman RM, Dutton DA, Howie HB. Subarachnoid anaesthesia for elective Caesarean section. A comparison of two hyperbaric solutions. *Anaesthesia* 1988; **43:** 96–9.
19. Seow LT, Lips FJ, Cousins MJ, Mather LE. Lidocaine and bupivacaine mixtures for epidural blockade. *Anesthesiology* 1982; **56:** 177–83.

*Anaesthesia*, 1989, Volume 44, pages 475–479

# Changes in cardiac output during epidural anaesthesia for Caesarean section

S. ROBSON, S. HUNTER, R. BOYS, W. DUNLOP AND M. BRYSON

## Summary

*Serial haemodynamic investigations were performed in 20 women who had epidural anaesthesia before elective Caesarean section. Cardiac output was measured by Doppler and cross-sectional echocardiography at the aortic valve. Measurements were performed after preloading the circulation with Ringer lactate solution (mean volume 805 ml) and then 10, 20, 30 and 40 minutes after administration of 0.5% bupivacaine. Preloading increased mean stroke volume from 84 to 94 ml and mean cardiac output from 7.01 to 7.70 litres/minute. Relative to basal values, mean arterial pressure decreased in all subjects after administration of bupivacaine (mean −14%, range −1 to −33%). Five subjects were given ephedrine because of hypotension. In three of these subjects hypotension was associated with a marked decrease in cardiac output. No significant changes in arterial blood pressure or cardiac output were demonstrated relative to basal values in the remaining 15 subjects. Ephedrine induced consistent increases in blood pressure and cardiac output.*

## Key words

*Anaesthetic techniques, regional*; epidural.
*Measurement techniques*; Doppler ultrasound, echocardiography.

The use of epidural anaesthesia for Caesarean section has increased in recent years. The haemodynamic changes associated with the extensive blockade necessary for surgery represent a potential hazard of the technique for mother and fetus.[1] Most previous studies have relied on blood pressure measurements to assess the cardiovascular effects of epidural block, and hypotension has been reported in 7–45% of subjects.[2,3] However, because of the likely alterations in peripheral resistance, changes in blood pressure do not necessarily reflect changes in maternal cardiac output and it is reductions in the latter which may pose the greatest risk to mother and fetus. Surprisingly little is known about the changes in cardiac output during epidural anaesthesia for Caesarean section.

Most previous studies have performed measurements of cardiac output after establishment of epidural anaesthesia adequate for surgery and after haemodynamic measurements have stabilised. Cardiac output in these circumstances has been reported to be increased,[4] decreased[5] and unchanged[6] relative to pre-anaesthetic levels. Ramanathan *et al.*[7] who used impedance cardiography measured cardiac output after induction of epidural anaesthesia to $T_{10}$ and then $T_6$. No significant changes in stroke volume or cardiac output were demonstrated. Measurements which use this technique correlate poorly with stroke volume measured by thermodilution during Caesarean section.[8] Thus there is a need for a serial study, using accepted methods, to investigate the haemodynamic changes during epidural anaesthesia for Caesarean section.

Cardiac output can be calculated from Doppler ultrasound measurement of aortic blood velocity combined with cross-sectional echocardiographic measurement of aortic orifice area. The technique has been validated in pregnancy[9] and allows reproducible noninvasive measurements of cardiac output.[10] We have used this technique to investigate serial changes in cardiac output after epidural administration of bupivacaine for Caesarean section.

## Methods

The study group consisted of 20 healthy women admitted

---

S.C. Robson, MRCOG, Research Registrar, W. Dunlop, PhD, FRCOG, Professor of Obstetrics, University of Newcastle, Princess Mary Maternity Hospital, Great North Road, Newcastle Upon Tyne, S. Hunter, FRCP, Consultant Paediatric Cardiologist, Freeman Hospital, Freeman Road, Newcastle Upon Tyne, R. Boys, PhD, BSc, Lecturer, Department of Statistics, University of Newcastle, Claremont Road, Newcastle Upon Tyne, M.R. Bryson, FFARCS, Consultant, Department of Anaesthesia, Princess Mary Maternity Hospital, Great North Road, Newcastle Upon Tyne.
Correspondence should be addressed to Prof. W. Dunlop please.

Accepted 31 October 1988.

0003–2409/89/060475 + 05 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

for elective Caesarean section at 38–39 weeks' gestation after an uncomplicated pregnancy. The details of the group are shown in Table 1. The procedure was explained to each subject and informed consent was obtained. The experimental protocol was approved by the Ethics Committee of Newcastle Health Authority. All subjects had an uncomplicated Caesarean section with a mean estimated blood loss of 600 ml (range 350–800 ml).

**Table 1.** Subject details. Values are expressed as mean (SD).

| | |
|---|---|
| Number | 20 |
| Nulliparous | 4 |
| Age, years | 27 (5) |
| Height, m | 1.53 (0.06) |
| Weight, kg | 56 (6) |
| Gestation at delivery, weeks | 38.6 (0.6) |
| Birth weight, kg | 3.29 (0.55) |

Each subject received oral ranitidine 150 mg on the evening before and on the morning of the operation together with sodium citrate 0.3 M (30 ml) on arrival in the operating theatre. Ringer lactate solution 500 ml was infused rapidly after insertion of an intravenous cannula. The infusion was then continued at a rate of 500 ml/15 minutes until the start of the operation and then 500 ml/30 minutes throughout the operation. An epidural catheter was introduced through a 16-gauge Tuohy needle at the $L_{2/3}$ or $L_{3/4}$ intervertebral space. A test dose of 0.5% bupivacaine 3 ml was given to exclude subarachnoid or intravascular administration. A further 10–17 ml (mean 12.5 ml) 0.5% bupivacaine was injected slowly with the subject in the right semilateral position in all cases after 5 minutes. The dose was determined with reference to the height of the patient: $< 1.50$ m, 10 ml; 1.51–1.60 m, 12–15 ml; $> 1.60$ m, 17 ml. The subject was turned to the left semilateral position after 10 minutes. Sensory block was assessed using the absence of perception of cold sensation to an ethyl chloride spray. Additional 0.5% bupivacaine (2–7 ml, mean 5 ml) was given if the sensory block was below $T_6$ at either 15 minutes ($n = 12$) or 25 minutes ($n = 5$). The top-up dose was determined by the block deficit. All subjects were given syntocinon 10 units intravenously at the time of delivery of the infant. Four were given intravenous opioids after delivery because of pain.

Arterial blood pressure was measured by an oscillotonometric technique using an automatic sphygmomanometer (Datascope Accutor 1). Measurements of systolic, mean and diastolic arterial pressure were obtained every minute. Hypotension was defined as a decrease in systolic pressure of $> 20\%$ of the pre-anaesthetic value. This was treated by increasing the rate of Ringer lactate infusion together with ephedrine 5–10 mg intravenously.

Investigations were performed in the operating theatre with the subject in the left semilateral position. Measurements were recorded before any intervention; after preloading with Ringer lactate solution; and at 10, 20, 30 and 40 minutes after administration of bupivacaine and before the start of surgery.

Aortic velocities were recorded with continuous wave Doppler ultrasound using a 2 MHz transducer (Vingmed) placed in the suprasternal notch. A spectrum analyser (Doptek) performed fast Fourier transform analysis of the Doppler signal and the output was converted to velocity of flow according to the Doppler equation:

$$V = \frac{f \times c}{2f_0 \times \cos\theta}$$

where V = velocity of erythrocytes, $f$ = Doppler frequency shift, $c$ = average speed of propagation of ultrasound in tissue, $f_0$ = emitting frequency of the transducer and $\theta$ = angle between the ultrasound beam and the direction of blood flow. The angulation of the transducer was adjusted until the highest velocities with the least spectral dispersion were obtained. These velocities were then stored in the spectrum analyser computer and it was assumed they represented the velocities at the aortic orifice and that the ultrasound beam was parallel with flow ($\cos\theta = 1$). The computer then calculated the heart rate and systolic velocity integral (area under the velocity curve) using 15/16 of the maximum frequency. This eliminated errors in the calculation of velocity integral from inclusion of high frequency interference. The average of 8–10 consecutive beats was used for each determination.

Aortic diameters were measured using a 5 MHz cross-sectional transducer (Ausonics). The aorta was imaged in the parasternal long axis plane and the orifice diameter was measured during systole.[10] The diameters from five consecutive beats were averaged and the cross-sectional area calculated from $\pi \times (D/2)^2$, where D = mean aortic orifice diameter. Cardiac output ($\dot{Q}_T$) was then calculated from the formula: $\dot{Q}_T$ (ml/minute) = heart rate (beats/minute) × stroke volume (ml) where stroke volume = velocity integral (cm) × cross-sectional area (sq cm). Blood pressure measurements were continued every minute during the echocardiographic investigations and the mean of three consecutive measurements was used for analysis.

Haemodynamic results before and after volume loading were compared using Student's paired $t$-test. Subsequent results in those subjects who did not require ephedrine were analysed with a repeated measures analysis of variance. The difference between time points was compared using the studentised range[11] at the 1% level because of the problem of multiple significance testing: (range = $q_{(v)} \times [\delta_R \div \sqrt{n}]$, where $q_{(v)}$ = critical value for comparing two time points, $\delta_R{}^2$ = residual mean square with $v$ degrees of freedom and n = number of subjects. Thus any change greater than the studentised range was considered statistically significant.

## Results

### *Haemodynamic changes during preloading with Ringer lactate solution*

The mean volume of fluid infused before haemodynamic measurements was 805 (range 600–1000) ml. The haemodynamic results are shown in Table 2. Preloading induced a significant increase in stroke volume because of an increase in velocity integral; there was no significant change in aortic area. Mean cardiac output increased 10% relative to basal values.

### *Haemodynamic changes during epidural blockade*

The mean total dose of 0.5% bupivacaine administered was 20 (SD 5) ml. Levels of sensory blockade achieved at 40 minutes were as follows: $T_2$ in three subjects, $T_3$ in one,

**Table 2.** Haemodynamic changes after preloading with a mean volume of 805 (range 600—1000) ml Ringer lactate solution ($n = 20$). Values are expressed as mean (SD).

| | Basal | After volume load | p |
|---|---|---|---|
| Heart rate, beats/minute | 83 (8) | 82 (7) | NS |
| Mean arterial pressure, mmHg | 86 (11) | 87 (11) | NS |
| Aortic area, sq cm | 4.14 (0.31) | 4.14 (0.33) | NS |
| Velocity integral, cm | 20.4 (1.5) | 22.8 (1.7) | < 0.001 |
| Stroke volume, ml | 84 (9) | 94 (10) | < 0.01 |
| Cardiac output/litres/minute | 7.01 (0.72) | 7.70 (0.84) | < 0.05 |

**Table 3.** Haemodynamic changes during establishment of epidural anaesthesia for Caesarean section in subjects who do not require ephedrine ($n = 15$).

| | | | After bupivacaine (minutes) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Basal | After volume load | 10 | 20 | 30 | 40 | SEM | SR |
| Heart rate, beats/minute | 84 | 83 | 84 | 83 | 83 | 85 | 2 | 6 |
| Mean arterial pressure, mmHg | 84 | 86 | 84 | 81 | 82 | 80 | 1 | 6 |
| Aortic area, sq cm | 4.16 | 4.16 | 4.14 | 4.09 | 4.08 | 4.09 | 0.02 | 0.08 |
| Velocity integral, cm | 20.2 | 22.6 | 21.4 | 22.0 | 21.1 | 20.5 | 0.3 | 0.7 |
| Stroke volume, ml | 84 | 94 | 89 | 90 | 86 | 84 | 1 | 6 |
| Cardiac output, litres/minute | 7.04 | 7.82 | 7.34 | 7.44 | 7.12 | 7.07 | 0.17 | 0.61 |

SEM, standard error of mean determined from analysis of variance; SR, studentised range.

$T_4$ in 10, $T_5$ in three and $T_6$ in three. The mean volume of Ringer lactate solution infused before surgery was 1870 (Range 1600–2200) ml. Five subjects required ephedrine for hypotension. The haemodynamic results in the remaining 15 subjects are shown in Table 3. There was no significant change in mean arterial pressure (MAP), relative to basal values, during establishment of epidural anaesthesia. However, there was a significant decrease between values obtained after preloading and those at 40 minutes after bupivacaine. Heart rate remained stable throughout the period of study. The decrease in aortic area at 30 minutes after bupivacaine just achieved statistical significance. Velocity integral increased after preloading and then decreased after administration of bupivacaine. Values remained elevated, relative to basal values, until 30 minutes after bupivacaine. Stroke volume and cardiac output decreased relative to values obtained after preloading, 30 minutes after administration of bupivacaine although there were no significant differences relative to basal values.

The changes in mean arterial pressure and cardiac output in the five subjects given ephedrine are shown in Figures 1 and 2. The lowest recorded arterial pressure and cardiac output after administration of bupivacaine in each

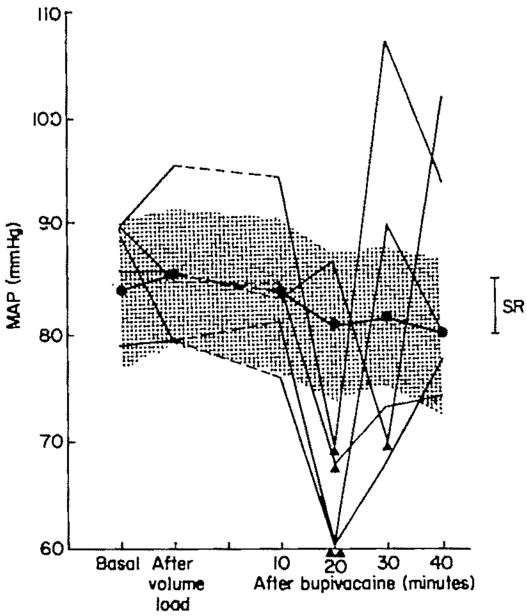


**Fig. 1.** Changes in mean arterial pressure (MAP) during epidural anaesthesia. ●, mean, and ▨, 99% confidence intervals for subjects not given ephedrine ($n = 15$); ——, individual data for subjects given ephedrine ($n = 5$); SR, studentised range; ▲, approximate time of administration of ephedrine.

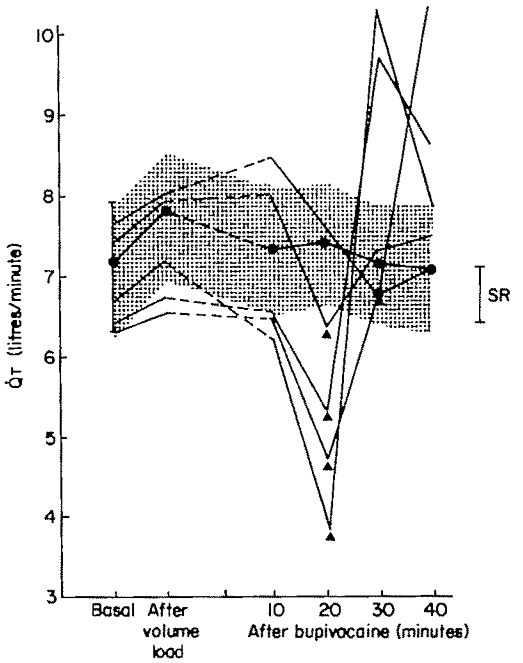


**Fig. 2.** Changes in cardiac output ($\dot{Q}_T$) during epidural anaesthesia. ●, mean, and ▨, 99% confidence intervals for subjects not given ephedrine ($n = 15$); SR, studentised range; ▲, approximate time of administration of ephedrine.

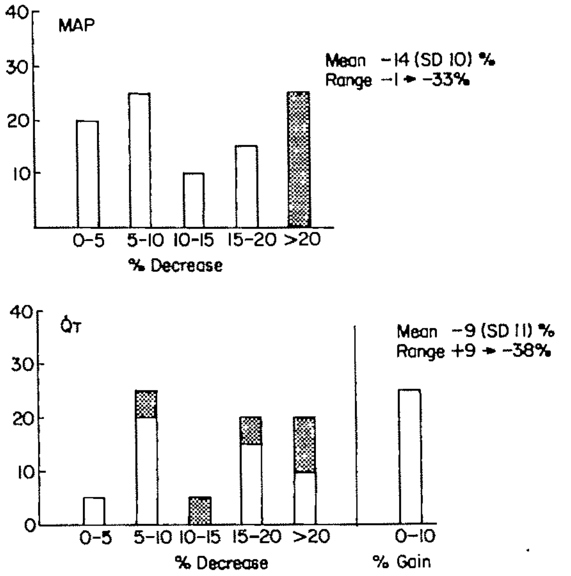


**Fig. 3.** Lowest recorded mean arterial pressure (MAP) and cardiac output ($\dot{Q}_T$) after administration of bupivacaine expressed as percentage of basal values ($n = 20$). ▨, subjects subsequently given ephedrine.

subject is shown in Figure 3. The magnitude of the haemodynamic change did not appear to be related to the level of block. The lowest recorded mean arterial pressure occurred at 10 minutes in one subject, 20 minutes in eight, 30 minutes in five and 40 minutes in six. The lowest recorded cardiac output occurred at 10 minutes in four subjects, 20 minutes in six, 30 minutes in five and 40 minutes in five. All subjects demonstrated a decrease in mean arterial pressure during establishment of epidural anaesthesia (mean −14%, range −1 to −33%). All mothers given ephedrine had a decrease in mean arterial pressure of more than 20%. The changes in cardiac output were less consistent (mean −9%, range +9 to −38%) and five subjects (25%) demonstrated a persistent elevation of cardiac output after administration of bupivacaine. It is apparent from Figure 3 that those who experienced the largest decrease in arterial pressure were not necessarily those who had the largest reductions in cardiac output. The decrease in blood pressure, in the five subjects who developed hypotension, did not appear to be related to the dose of bupivacaine administered (mean 22 ml, range 15–27 ml) or to the level of block ($T_6$ in one, $T_4$ in three and $T_2$ in one).

The individual changes in mean arterial pressure, heart rate, stroke volume and cardiac output within 5 minutes of administration of ephedrine, expressed as a percentage of the pretreatment value, are shown in Table 4. Hypotension was associated with a bradycardia (62 beats/minute) in one subject and she was given atropine 0.3 mg intravenously at the same time as ephedrine. There was a consistent increase in heart rate, cardiac output and mean arterial pressure after administration of ephedrine.

## Discussion

The Doppler echocardiographic methods used in this study were validated against the Fick technique by the authors[10] and measurements of cardiac output using this technique correlate closely with cardiac output measured by thermodilution during pregnancy.[9] The within-subject and hour-to-hour coefficients of variation of the technique are less than 5%,[10] which suggests that the method is suitable for studying serial changes in cardiac output in pregnant subjects. The values obtained for basal cardiac output in the left lateral position are comparable to those previously reported by us at 38–40 weeks' gestation[12] and are within the range reported by other workers.[13,14]

**Table 4.** Haemodynamic changes associated with intravenous ephedrine. Measurements were made within 5 minutes of administration and results are quoted as percentage change from pre-ephedrine values.

| Subject | Dose (mg) | Cardiac output | Stroke volume | Heart rate | Mean arterial pressure |
|---|---|---|---|---|---|
| | | (% change) | | | |
| 1 | 5 | +17 | −18 | +42 | +13 |
| 2* | 10 | +157 | +38 | +87 | +56 |
| 3 | 10 | +45 | +7 | +22 | +50 |
| 4 | 10 | +56 | +15 | +37 | +48 |
| 5 | 10 | +85 | +57 | +18 | +15 |

* This subject also received intravenous atropine 0.3 mg.

This appears to be the first study to report the haemodynamic effects of an intravenous infusion of Ringer lactate solution before epidural anaesthesia in obstetric patients. The results suggest that infusion of approximately one litre of crystalloid solution increases stroke volume and cardiac output. The increase in stroke volume almost certainly reflects an increase in venous return. The elevation in central venous pressure after infusion of 2 litres of crystalloid solution and establishment of epidural block lends support to this.[3]

A decrease in systolic arterial blood pressure of greater than 20% occurred in 25% of subjects after epidural blockade. Previous studies, which have used a similar definition, have reported hypotension in 25–45% of subjects[2,15,16] Lewis *et al.*[3] suggested that the incidence of hypotension was related to the volume of preload administered. A lower incidence of hypotension might have been achieved if bupivacaine had been administered using an incremental regimen.[17,18]

Epidural anaesthesia was associated with haemodynamic stability in those subjects not given ephedrine. Few previous studies have performed serial haemodynamic measurements after the start of epidural anaesthesia and before surgery. Maruta[5] measured cardiac output using M-mode echocardiography before and 15 minutes after epidural anaesthesia (2% mepivacaine 7–10 ml). They suggested mean stroke volume decreased by 19%. The smaller decrease in stroke volume in the present study may be explained by the larger volume of Ringer lactate solution. Ramanathan *et al.*[7] induced epidural anaesthesia up to $T_6$ by injecting lignocaine 1.5% with adrenaline 1:200 000 in 5-ml increments. Cardiac output was measured with impedance cardiography when anaesthesia had reached $T_{10}$ and then again at $T_6$. No significant change in stroke volume or cardiac output was demonstrated in subjects not given ephedrine (70%), although there was an increase in heart rate. All other workers have repeated haemodynamic investigations after attainment of surgical anaesthesia and haemodynamic stability. In the nonpregnant subject epidural blockade to a comparable level used during Caesarean section has been reported to result in alterations in cardiac output of between +2% and −17%.[19–21]

Ephedrine, when administered to subjects with hypotension, induced consistent increases in blood pressure and cardiac output. These findings confirm those of Ramanathan *et al.*[7] who administered ephedrine to 30% of subjects because of hypotension and reported an increase in mean cardiac output of 35%. This was due to an increase in stroke volume, since there was a significant decrease in heart rate. Ephedrine appeared to increase heart rate as well as stroke volume in our subjects. Ephedrine induces consistent increases in blood pressure and cardiac output secondary to vasoconstriction and an augmentation of myocardial contractility (providing venous return is adequate) in nonpregnant subjects. The effect on heart rate is more variable.[22]

The rapid and in some cases marked haemodynamic effects of ephedrine were well tolerated in our subjects. This may not be the case in subjects with cardiac disease particularly when cardiac output is relatively fixed for instance in mitral stenosis. The incidence and unpredictability of hypotension shown in this study may influence the choice of anaesthetic for cardiac patients who require Caesarean section.

### Acknowledgments

The work was supported by a grant from Birthright.

### References

1. Ralston DH, Shnider SM. The fetal and neonatal effects of regional anesthesia in obstetrics. *Anesthesiology* 1978; **48:** 34–64.
2. Hallworth D, Jellicoe JA, Wilkes RG. Hypotension during epidural anaesthesia for Caesarean section. A comparison of intravenous loading with crystalloid and colloid solutions. *Anaesthesia* 1982; **37:** 53–6.
3. Lewis M, Thomas P, Wilkes RG. Hypotension during epidural analgesia for Caesarean section. Arterial and central venous pressure changes after acute intravenous loading with two litres of Hartmann's solution. *Anaesthesia* 1983; **38:** 250–3.
4. Milsom I, Forssman L, Biber B, Dottori O, Rydgren B, Sivertsson R. Maternal haemodynamic changes during Caesarean section: a comparison of epidural and general anaesthesia. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 161–7.
5. Maruta S. The observation of the maternal hemodynamics during labor and Cesarean section. *Nippon Sanki Fujinka Gakkai Zasshi* 1982; **34:** 776–84.
6. Ueland K, Akamatsu TJ, Eng M, Bonica JJ, Hansen JM. Maternal cardiovascular dynamics VI. Cesarean section under epidural anesthesia without epinephrine. *American Journal of Obstetrics and Gynecology* 1972; **114:** 775–80.
7. Ramanathan S, Grant G, Turndorf H. Cardiac preload changes with ephedrine therapy for hypotension in obstetrical patients. *Anesthesia and Analgesia* 1986; **65:** S125.
8. Secher NJ, Arnsbo P, Heslet Anderson L, Thomsen A. Measurements of cardiac stroke volumes in various body positions in pregnancy and during Caesarean section: a comparison between thermodilution and impedance cardiography. *Scandinavian Journal of Clinical and Laboratory Investigation* 1979; **39:** 569–76.
9. Easterling TR, Watts DH, Schmucker BC, Benedetti TJ. Measurement of cardiac output during pregnancy: validation of Doppler technique and clinical observations in preeclampsia. *Obstetrics and Gynecology* 1987; **69:** 845–50.
10. Robson SC, Dunlop W, Moore M, Hunter S. Combined Doppler and echocardiographic measurement of cardiac output: theory and application in pregnancy. *British Journal of Obstetrics and Gynaecology* 1987; **94:** 1014–27.
11. Pearson ES, Hartley HO. *Biometrika tables for statisticians.* London: Cambridge University Press, 1966.
12. Robson SC, Hunter S, Moore M, Dunlop W. Haemodynamic changes during the puerperium: a Doppler and M-mode echocardiographic study. *British Journal of Obstetrics and Gynaecology* 1987; **94:** 1028–39.
13. Vorys N, Ullery JC, Hanusek GE. The cardiac output changes in various body positions in pregnancy. *American Journal of Obstetrics and Gynecology* 1961; **82:** 1312–21.
14. Kjeldsen J. Hemodynamic investigations during labour and delivery. *Acta Obstetrica et Gynaecologica Scandinavica* 1979; **89:** 1–252.
15. Antoine C, Young BK. Fetal lactic acidosis and epidural anesthesia. *American Journal of Obstetrics and Gynecology* 1982; **142:** 55–9.
16. Laishley RS, Morgan BM. A single dose epidural technique for Caesarean section. A comparison between 0.5% bupivacaine plain and 0.5% bupivacaine with adrenaline. *Anaesthesia* 1988; **43:** 100–3.
17. Thorburn J, Moir DD. Epidural analgesia for elective Caesarean section. Technique and its assessment. *Anaesthesia* 1980; **35:** 3–6.
18. Crawford JS, Davies P, Lewis M. Some aspects of epidural block provided for elective Caesarean section. *Anaesthesia* 1986; **41:** 1039–46.
19. Ward RJ, Bonica JJ, Freund FG, Akamatsu T, Danzunger F, Englesson S. Epidural and subarachnoid anesthesia. Cardiovascular and respiratory effects. *Journal of the American Medical Association* 1965; **191:** 99–102.
20. Bonica JJ, Berges PU, Morikawa K. Circulatory effects of peridural block I. Effects of level of analgesia and dose of lidocaine. *Anesthesiology* 1970; **33:** 619–26.
21. Scott DB, Littlewood DG, Drummond GB, Buckley PF, Covino BG. Modification of the circulatory effects of extradural block combined with general anaesthesia by the addition of adrenaline to lignocaine solutions. *British Journal of Anaesthesia* 1977; **49:** 917–25.
22. Goodman M, Gilman A, Goodman LS, comps. *The pharmacological basis of therapeutics*, 6th edn. New York: Macmillan Publishing 1980: 163.

*Anaesthesia*, 1989, Volume 44, pages 480–482

# Inheritance of low plasma cholinesterase activity in two families with a history of suxamethonium sensitivity

M. WHITTAKER, M. BERRY AND J. J. BRITTEN

## Summary

*An hypothesis advanced in 1970 concerning family inheritance of low enzymic activities of plasma cholinesterase has been substantiated. The recognition of three* $E_1^kE_1^s$ *genotypes is reported in this family after investigation of a new generation. A second family with similar genetic characteristics is described.*

**Key words**

*Enzymes*; cholinesterase.
*Neuromuscular blockers*; suxamethonium.

In 1970 we published our initial experiences of the Cholinesterase Research Unit.[1] Some of our biochemical data were difficult to interpret at that time and yet their validity was consolidated by family back-up. We had received several specimens which had the usual phenotype but with enzymic activity well below the range for the genotype $E_1^uE_1^s$. Repeat samples confirmed our data and none of the physiological, pathological or iatrogenic causes for a decreased cholinesterase activity[2] was apparent. Family studies made it unlikely that these individuals could be homozygous for the silent gene. We tentatively suggested a low activity gene of normal phenotype and recommended follow-up studies to test the validity of our hypothesis. We illustrated our findings with a family in which the propositus was an 8-year-old boy who had genotype $E_1^sE_1^s$. We have re-examined this family and present an interpretation of our results which confirms our original hypothesis. A second family with similar findings is also reported in which the propositus was a silent homozygote $E_1^sE_1^s$.

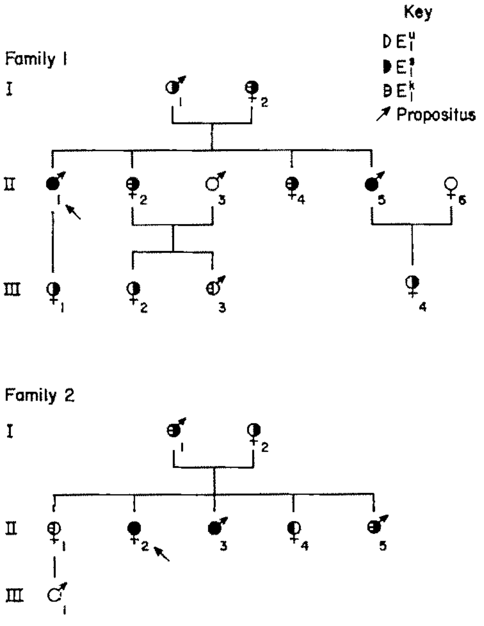


**Fig. 1.** Pedigrees of the two families investigated.

### Materials and methods

Heparinised blood samples (10 ml) were obtained from members of two families (Fig. 1) with a history of suxamethonium sensitivity. Each sample was phenotyped by determining dibucaine (DN) and fluoride (FN) numbers using $5 \times 10^{-5}$ M benzoylcholine as substrate.[3] The RO2-0683 [dimethylcarbamate of (2-hydroxy-5 phenylbenzyl) trimethylammonium bromide] numbers (RO2N) were measured at 25°C, in duplicate, using the same substrate and RO2-0683 ($10^{-8}$M) as differential inhibitor. The method was a modification of that of Liddell *et al.*[4] but identical to that used by Evans and Wardell.[5]

---

M. Whittaker, MSc, PhD, DSc, Department of Chemistry, University of Exeter, EX4 4QD, M. Berry, MB, ChB, FFARCSI, Hartlepool General Hospital, Hartlepool, Cleveland, TS24 9AH, J.J. Britten, MSc, Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS.

Accepted 5 December 1988.

0003–2409/89/060480 + 03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Biochemical data for two families with low plasma cholinesterase activity.

| Family | Individual | Sex | Age (years) | Enzymic activity* 1970 | Enzymic activity* 1988 | Dibucaine number | Fluoride number | RO2N (see text) |
|---|---|---|---|---|---|---|---|---|
| 1 | $I_1$ | M | 55 | 0.61 | 0.55 | 82 | 62 | 90 |
|  | $I_2$ | F | 52 | 0.31 | 0.38 | 78 | 62 | 91 |
|  | $II_1$** | M | 32 | 0.04 | 0.02 | 79 | 61 | 95 |
|  | $II_2$ | F | 30 | 0.31 | 0.35 | 83 | 60 | 90 |
|  | $II_3$ | M | 32 | — | 1.11 | 80 | 57 | 92 |
|  | $II_4$ | F | 29 | 0.31 | 0.18 | 79 | 61 | 94 |
|  | $II_5$ | M | 28 | 0.05 | 0.03 | 79 | 61 | 94 |
|  | $II_6$ | F | 27 | — | 1.25 | 79 | 62 | — |
|  | $III_1$ | F | 8 | — | 0.64 | 81 | 58 | 94 |
|  | $III_2$ | F | 11 | — | 0.53 | 80 | 57 | 92 |
|  | $III_3$ | M | 6 | — | 1.03 | 78 | 58 | 94 |
|  | $III_4$ | F | 2 | — | 0.82 | 80 | 62 | — |
| 2 | $I_1$ | M | — | — | 0.21 | 79 | 65 | — |
|  | $I_2$ | F | — | 0.77 | 0.59 | 80 | 59 | — |
|  | $II_1$ | F | — | — | 0.71 | 80 | 58 | 91 |
|  | $II_2$** | F | — | — | 0.02 | — | — | — |
|  | $II_3$ | M | — | — | 0.02 | — | — | — |
|  | $II_4$ | F | — | — | 0.61 | 82 | 60 | — |
|  | $II_5$ | M | — | — | 0.28 | 80 | 57 | — |
|  | III | M | — | — | 0.94 | 79 | 57 | 94 |

* μmol benzoylcholine hydrolysed/minute/ml of plasma.
** propositus.

**Table 2.** Biochemical data from individuals with $E_1^kE_1^s$ genotype compared with similar parameters for the usual phenotype $E_1^uE_1^u$.

|  | Enyzmic activity* | Dibucaine number | Fluoride number | RO2N (see text) |  |
|---|---|---|---|---|---|
|  | 0.39 | 80 | 59 | 89 | Whittaker *et al.*[6] |
|  | 0.39 | 81 | 58 | 90 | Whittaker *et al.*[6] |
|  | 0.33 | 83 | 62 | 99 | Whittaker *et al.*[6] |
|  | 0.28 | 80 | 60 | 89 | Whittaker *et al.*[6] |
|  | 0.47 | 79 | 56 | 100 | Whittaker *et al.*[6] |
|  | 0.38 | 79 | 60 | 100 | Whittaker *et al.*[6] |
|  | 0.43 | 82 | 60 | 100 | Whittaker and Britten[7] |
|  | 0.39 | 81 | 61 | — | Whittaker and Britten[7] |
|  | 0.35 | 78 | 62 | 91 | Present study |
|  | 0.33 | 83 | 60 | 90 | Present study |
|  | 0.31 | 79 | 61 | 94 | Present study |
| Mean (SD) of 11 individuals | 0.37 (0.05) | 80.50 (1.69) | 59.90 (1.76) | 94.20 (4.98) |  |
| Mean (SD) for $E_1^uE_1^u$ | 1.03 (0.18) | 80.10 (1.56) | 61.35 (3.21) | 94.40 (2.05) |  |

* μmol benzoylcholine hydrolysed/minute/ml of plasma.

## Results

Table 1 records the enzymic activity, dibucaine, fluoride and RO2 numbers for each member of Family 1 found in 1988 and additionally, the enzymic activities of the individuals tested in 1970. Similar data for a second family are included also in Table 1.

The available data for the genotype $E_1^kE_1^s$ are shown in Table 2.

## Discussion

All individuals in Family 1 have the usual phenotype, as their inhibition characteristics fall within the ranges quoted for the usual enzyme $E_1^uE_1^u$; however, their enzymic activities show considerable variation. The extremely low cholinesterase activity of the propositus $II_1$ and one of his siblings $II_5$ has been confirmed in our present samples. These results not only confirm that $II_1$ and $II_5$ are silent homozygotes $E_1^sE_1^s$ but indicate that both the father $I_1$ and mother $I_2$ must carry a silent gene $E_1^s$. The significant difference in enzymic activities between the two parents has been confirmed in the newer samples.

Our normal range of activities for the usual genotype $E_1^uE_1^u$ is 0.8–1.2 μmol benzoylcholine hydrolysed per minute per millilitre of plasma. Each gene must contribute equally to this activity within the range 0.4–0.6 units. The silent gene $E_1^s$ makes little contribution to the overall activity. We can therefore assume that the mean activity of the genotype $E_1^uE_1^s$ falls within the range 0.4–0.6 units. It is clear that the activity of $I_1$ falls within this range and so the proposed genotype of $E_1^uE_1^s$ is acceptable. The activity of his wife, who is very fit and not taking any drugs, is lower than one would expect for the same genotype.

Rubinstein *et al.*[8] recognised, by unusual dibucaine numbers, a new allelle $E_1^k$ for plasma cholinesterase in two families segregating the $E_1^s$ gene. This enabled them to identify the $E_1^sE_1^k$ genotype but, in the absence of the $E_1^s$ gene, the other genotypes gave identical inhibition characteristics to the usual genotype $E_1^uE_1^u$. Rubinstein and his co-workers indicated a 33% reduction in enzymic activity when the $E_1^u$ gene is replaced by an $E_1^k$ gene. This information enables us to deduce that the $E_1^k$ gene should be associated with activity in our laboratory in the range of 0.26–0.40 units (i.e. 66% of the activity of the usual gene). The activity of the genotype $E_1^kE_1^s$ could be expected to be in this range and the mother $I_2$ of the propositus $II_1$ could have this genotype as it is obligatory that she carries a silent gene. Our earlier study showed that the biochemical data for the mother $I_2$ and two of her children $II_2$ and $II_4$ were identical and that they must therefore have the same genotype. The present study confirms that $I_2$ and $II_2$ are very similar and are probably genotype $E_1^kE_1^s$. The enzymic activites of these two women are within the range recorded for the individuals who have been shown by genetic analysis to have the $E_1^kE_1^s$ genotype (Table 2).

The younger daughter $II_4$ shows a marked decrease in enzymic activity between the first and second samples. We have taken a third sample from the sisters $II_2$ and $II_4$ and confirmed their current activities. Both are healthy young women. We now find that wheareas $II_2$ is having no medication, $II_4$ is taking oral contraceptives. These drugs are known to decrease plasma cholinesterase activity[2] and so we can safely assume that she probably has the genotype $E_1^kE_1^s$.

It is useful that we have a new generation on which to test the assigned genotypes in this family study. One must also be aware that cholinesterase activity varies considerably with age in children. It appears to be maximum at about 6 years[9] and thereafter decreases gradually until puberty, when it reaches the adult level. $III_1$ must have an $E_1^s$ gene and her lowish activity is consistent with an $E_1^uE_1^s$ genotype. $III_2$ also has the same genotype but $III_3$ has too high an activity to have the silent gene and so he must be an obligatory $E_1^uE_1^k$ because his mother is $E_1^kE_1^s$ and his father $II_3$ has the usual genotype. Although the cholinesterase activity of $III_3$ falls within the normal range for the $E_1^uE_1^u$ genotype, it has been shown by Whittaker and Britten[10] that 38 obligatory $E_1^uE_1^k$ genotypes from 47 families average 91% (SD 20) of the usual activity. By using the 33% reduction produced by an $E_1^k$ gene, we can calculate an approximate range of enzymic activity for the genotype $E_1^uE_1^k$ as 0.66–1.00 units. This range of activity has considerable overlap with that for the usual genotype and so the enzymic activity of $III_3$, a young boy, is not at variance with the genotype $E_1^uE_1^k$. The 2-year-old girl $III_4$ must have genotype $E_1^uE_1^s$ because her mother has the usual genotype and her father is a silent homozygote. It is acknowledged that neonates have low cholinesterase activity but normal values are reached within the first month of life[11] and the activity increases during early childhood.[7] It is therefore not surprising that the cholinesterase activity of $III_4$ is high for her obligatory $E_1^uE_1^s$ genotype; at puberty her activity could be within the range 0.40–0.60 units in our laboratory.

In Family 2 the propositus $II_2$ and one of her siblings $II_3$ are $E_1^sE_1^s$ homozygote and so both parents $I_1$ and $I_2$ must be segregating the $E_1^s$ allele. Inhibition studies show that with the exception of $II_2$ and $II_3$, the remaining members of this family have the usual phenotype. The biochemical data indicate that $I_2$ and $II_4$ must have the same genotype and are probably $E_1^uE_1^s$.

Individual $II_1$ could have this genotype but her higher activity is more akin to genotype $E_1^uE_1^k$ for which our theoretical range of activity is 0.66–1.00 units. The biochemical data for $I_1$ and $II_5$ suggest that these two individuals should have the same genotype. One must consider whether the $E_1^J$ allele[12] is segregating in this family. This allele is associated with only 33% of the usual enzymic activity and an $E_1^JE_1^s$ genotype would be expected to have an activity of 0.13–0.20 units in our laboratory. Whereas $I_1$ could have this genotype, it is not so likely for his daughter $II_5$ who is a mature woman. Although it seems probable that $I_1$ and $II_5$ have the genotype $E_1^kE_1^s$ and both will be sensitive to suxamethonium their biochemical data are not included in Table 2.

The recognition of the genotype $E_1^kE_1^s$ in three members of Family I substantiates our 1970 hypothesis of a low activity gene of normal phenotype. It is the $E_1^k$ gene described by Rubinstein *et al.*[6] in 1978. All three $E_1^kE_1^s$ individuals will be sensitive to suxamethonium.

## Acknowledgments

Financial support from the Northcott Devon Medical Foundation (M.W.) and the Department of Health and Social Security (J.J.B.) is gratefully acknowledged. Family I was referred initially by Dr P. Trider of Sunderland, to whom we are indebted.

## References

1. Whittaker M, Vickers MD. Initial experiences with the Cholinesterase Research Unit. *British Journal of Anaesthesia* 1970; **42:** 1016–20.
2. Whittaker M. Plasma cholinesterase and the anaesthetist. *Anaesthesia* 1980; **35:** 174–97.
3. Whittaker M. Cholinesterase In: Beckman L, ed. *Monographs in human genetics Vol. 11.* Basel: Karger, 1986: 1–125.
4. Liddell J, Newman GE, Brown DF. A pseudocholinesterase variant in human tissues. *Nature* 1963; **198:** 1090–1.
5. Evans RT, Wardell J. On the identification and frequency of the J and K cholinesterase phenotypes in a Caucasian population. *Journal of Medical Genetics* 1984; **21:** 99–102.
6. Whittaker M, Britten JJ. Vyas AB, Hayes TC. Family studies of the $E_1^kE_1^s$ genotype for plasma cholinesterase. *Human Heredity* 1988; **38:** 228–32.
7. Whittaker M, Britten JJ. Recognition of two new phenotypes segregating the $E_1^k$ allele for plasma cholinesterase. *Human Heredity* 1988: **38:** 233–9.
8. Rubinstein HM, Dietz AA, Lubrano T. $E_1^k$, another quantitative variant at cholinesterase locus 1. *Journal of Medical Genetics* 1978; **15:** 27–9.
9. Dabew D. Cholinesterase und Transaminase Aktivitat im Serum von Kindern (3 bis 6 Jahre alt) *Zeitschrift für Klinische Chemie und Klinische Biochemie* 1970; **8:** 12–6. Cholinesterase and transaminase activities in the serum of children (3 to 6 years old) [English title].
10. Whittaker M, Britten JJ. Plasma cholinesterase variants. Family studies of the $E_1^k$ gene. *Human Heredity* 1985; **35:** 364–8.
11. Rasore-Quartino A, Reali S, Baldi M, Tassara P, Tessitore L, Schiavetti P. Modificazione dell'atività della colinesterasi sierica nel neonato e nel lattante. Atti Convegno congiunto AIGM e AICM Torino 3-5 marzo 1983. *Pathologica* 1983; **75:** (Suppl.): 75–6.
12. Garry PJ, Dietz AA, Lubrano T, Ford PC, James K, Rubinstein HM. New allele at cholinesterase locus 1. *Journal of Medical Genetics* 1976; **13:** 38–42.

*Anaesthesia*, 1989, Volume 44, pages 483–484

CASE REPORT

# 'Locked-in' syndrome

## Occurrence after coronary artery bypass graft surgery

D. J. KENNY AND D. A. LUKE

**Summary**

*The 'locked-in' syndrome has not previously been described in the immediate period after open-heart surgery. We describe the case of a patient who remained tetraplegic and mute, but alert, after graft surgery. A brief review of the aetiological factors in the development of this type of stroke after coronary artery bypass is presented.*

**Key words**

*Complications*; neurological.
*Surgery*; cardiovascular.

The term 'locked-in' syndrome was initially used by Plum and Posner in 1972[1] to describe the tetraplegic, mute, but full alert state that results when the descending motor pathways are interrupted by infarction of the ventral pons. Such patients are entirely awake, responsive and sentient, although their repertory of responses is limited to blinking and jaw and eye movements. We describe a case after open-heart surgery.

### Case history

A 56-year-old male presented to the hospital with a 4-hour history of central chest tightness radiating to both shoulders. He had no history of diabetes, hypertension or transient ischemic attacks. Physical examination was normal; there was no evidence of generalised atherosclerosis. Serial electrocardiograms showed changes of an acute inferior myocardial infarction and cardiac enzymes were significantly elevated. He was treated with nifedipine, glyceryl trinitrate and subcutaneous heparin.

Ten days later he underwent coronary angiography. This showed a blocked proximal left anterior descending artery with distal refill, a blocked right coronary artery with distal refill and good left ventricular function.

He developed unstable angina the next day. Two days later he underwent urgent coronary artery bypass graft surgery. There was no obvious evidence of infarction at surgery. Nonpulsatile hypothermic (26°C) cardiopulmonary bypass was established using aortic and single venous cannulae and no vent at a flow rate of 2.4 litres/sq m/minute. Arterial pressure was 60 mmHg. A membrane oxygenator and an arterial filter were used. Three-vessel grafts were carried out without problem. The patient came off bypass easily; there was a bradycardia which responded to atropine and a bolus of isoprenaline.

We noted that he did not move his limbs but that he opened his eyes to simple commands during the first 24 hours after operation. His pupils were equal and reacting; he opened and closed his eyes to command. He could not cough and his trachea remained intubated, but he was breathing spontaneously. He had no power in all four limbs in which tone was increased and his deep tendon reflexes were symmetrically increased. He had bilateral upgoing plantar responses and a withdrawal reflex to painful stimuli. Subsequent investigations included a negative edrophonium test and a normal electroencephalogram, lumbar puncture and computerised axial tomography scan.

Three months later despite intensive physiotherapy the patient remains mute and tetraplegic; he has no control over his palate and tongue, he is able to communicate via eye movements and has had minimal return of power to his right arm and leg.

### Discussion

The 'locked-in' syndrome is an uncommon type of cerebrovascular accident and as such was not fully recognised in our patient until 48 hours after the operation. Such patients are fully conscious although they are often assumed to be in coma; consequently they may be distressed by conversation around them.

Our patient met all the clinical criteria for the 'locked-in' syndrome as described by Plum and Posner. Their patient, a 44-year-old white male had a complete occlusion of his basilar artery.[1] The patient was awake but had lost all

---

D.J. Kenny, MB, MRCPI, Registrar in Cardiology, D.A. Luke, MB, FRCSI, Consultant Cardiothoracic Surgeon, Department of Cardiology, Royal City of Dublin Hospital, Baggot St, Dublin 4, Ireland.

Accepted 19 October 1988.

0003–2409/89/060483 + 02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

power to communicate except with his eyes. Like M. Noirtier de Villefort in Dumas' *The Count of Monte Cristo* he was 'a corpse with living eyes'. This syndrome usually results from demyelination, haemorrhage or infarction of the ventral pons or medulla. Retention of consciousness depends on the sparing of the upper pontine tegmentum above the level of the trigeminal nucleus; the lesion paralyses the pyramidal tracts to the limbs and the lower cranial nerves.[2] Patients with the 'locked-in' syndrome are akinetic and mute, but they do not suffer from akinetic mutism in which condition patients lie motionless and mindless and can make no appropriate response.[2] In one unusual case in which the 'locked-in' syndrome persisted for over 2 years, the patient learned to communicate via morse code, using eye blinks and jaw movements.[3]

The cause of the lesion in our patient is unclear as are the cerebral consequences of cardiopulmonary bypass.[4] Central pontine myelinolysis is unlikely in our patient because he had no history of alcohol abuse or hyponatraemia.[5] Haemorrhage is also unlikely since he had no evidence of a coagulopathy and postmortem results in the 'locked-in' syndrome are consistent with infarction.[6] Infarction as a result of thrombosis due to pre-existing disease is also unlikely since even pre-existing cerebrovascular disease is not predictive of the postoperative neurological deficit, also these cases resulted from low perfusion pressure and long bypass time which was not the case in our patient.[7]

The 'locked-in' syndrome due to thrombo-embolism of the basilar artery is also described 8 months after aortic valve replacement with a Bjork-Shiley prosthesis.[8] That case was probably caused by thrombo-embolism from the prosthetic valve.

We consider that embolism to the basilar artery was the probable cause in our patient. Micro-embolism in the territory of the internal carotid artery during cardiopulmonary bypass is well-recognised[9] and histopathological studies have demonstrated platelet-fibrin microemboli in the brains of patients who died after bypass.[10] Our patient was at risk of embolus from a mural thrombus because of his recent myocardial infarct, although it is impossible to exclude embolism from other sources. Recovery from the 'locked-in' syndrome is described;[11] it is unusual and most cases eventually deteriorate and die.

## References

1. PLUM F, POSNER JD. *Diagnosis of stupor and coma*, 2nd edn. Philadelphia: F.A. Davis, 1972.
2. EDITORIAL. The locked-in syndrome. *British Medical Journal* 1987; **294**: 198–9.
3. FELDMAN MH. Physiological observations in a chronic case of 'locked-in' syndrome. *Neurology* 1971; **21**: 459–78.
4. EDITORIAL. Brain damage after open-heart surgery. *Lancet* 1982; **1**: 1161–3.
5. STERNS RN, RIGGS JE, SCHOCHET SS. Osmotic demyelination syndrome following correction of hyponatremia. *New England Journal of Medicine* 1986; **314**: 1535–42.
6. HAWKES CH. 'Locked-in syndrone': report of seven cases. *British Medical Journal* 1974; **4**: 379–82.
7. SMITH PLC, TREASURE T, NEWMAN SP, JOSEPH P, ELL PJ, SCHNEIDAU A, HARRISON MJG. Cerebral consequences of cardiopulmonary bypass. *Lancet* 1986; **1**: 823–5.
8. OTTOMO M, OKADA Y, DAIOOHJI S. ['Locked-in syndrome' after aortic valve replacement with Bjork-Shiley prosthesis—report of a case (author's translation)]. *Nippon Kyobu Geka Gakkai Zasshi* 1981; **29**: 1944–7.
9. BLAUTH C, KOHZNER EM, ARRNOLD J, TAYLOR KM. Retinal microembolism during cardiopulmonary bypass demonstrated by fluorescein angiography. *Lancet* 1986; **2**: 837–9.
10. HILL JD, AGUILAR MJ, BARANCO A, LANEROLLE P DE, GERBODE F. Neuropathological manifestations of cardiac surgery. *Annals of Thoracic Surgery* 1969; **7**: 409–19.
11. BUCHMAN AS, WICHTER MD. Recovery following the 'locked-in' syndrome. *Stroke* 1986; **17**: 558 (letter).

*Anaesthesia*, 1989, Volume 44, pages 485–486

CASE REPORT

# Atracurium overdose in a small infant

A. J. CHARLTON, N. J. N. HARPER, D. EDWARDS AND A. C. WILSON

**Summary**

*An error in setting a syringe driver caused a 2.75 kg infant to receive 37 mg atracurium over 75 minutes. Clinically full recovery of muscle power had returned spontaneously 135 minutes after the infusion was stopped. The child suffered no ill effects. Assay of blood and urine for atracurium and laudanosine confirmed rapid clearance of the drug.*

**Key words**

*Neuromuscular relaxants*; atracurium.
*Complications*; overdose.

The short action, rapid offset and spontaneous breakdown of atracurium makes it a particularly attractive drug for use in neonates and small infants who require prolonged mechanical ventilation. We report a case in which an inadvertent overdose of atracurium in an infant demonstrated its remarkable lack of toxicity.

## Case history

A 2.75 kg infant aged 59 days presented for dilatation of oesophageal stricture, secondary to neonatal oesophageal atresia repair. She received 2.5 mg atracurium during an uneventful anaesthetic that lasted 75 minutes. Respiratory and cardiovascular collapse occurred at 3.5 hours after operation and she required a rapid 20-ml infusion of plasma, tracheal intubation and intermittent positive pressure ventilation of her lungs. Chest radiography was unhelpful and IPPV was continued. A total of atracurium 3 mg had been given 30 minutes after the collapse to accomplish nasotracheal intubation, and 45 minutes later an infusion was started, made up with atracurium 50 mg in 50 ml sterile water to commence at an intended rate of 1 ml/hour. It was discovered about half an hour later that the syringe driver was set at 61 ml/hour and that the patient had already received 34 ml of solution.

The child was noted to be flushed but not hypotensive. There was neither bradycardia nor bronchospasm. Arterial blood pressure remained elevated by about 20 mmHg systolic at 99/55 mmHg during the period of neuromuscular blockade. Just 2 hours after stopping the infusion, over a period of 15 minutes, spontaneous breathing and then limb movements returned. Morphine 0.5 mg was given to assist control of ventilation, but 2 hours later the patient extubated her own trachea. There were no sequelae.

Urine and plasma samples were taken the next morning for estimation of atracurium and laudanosine levels with an established HPLC assay.[1] Sensitivity of the assay is 0.2 $\mu$g/ml for atracurium and 0.01 $\mu$g/ml for laudanosine. The results are shown in Tables 1 and 2.

**Table 1.** Plasma concentrations ($\mu$g/ml) at times after cessation of atracurium infusion.

| Time (hours) | Atracurium | Laudanosine |
|---|---|---|
| 11.3 | 0 | 0.59 |
| 14.5 | 0 | 0.18 |
| 17.3 | 0 | 0 |

**Table 2.** Total excretion ($\mu$g) in urine collected during periods timed from cessation of atracurium infusion.

| Collected period (hours) | Atracurium | Laudanosine |
|---|---|---|
| 0–11.3 | 1394 | 6847 |
| 11.3–17.3 | 0 | 59 |
| At 24 | 0 | 0 |

## Discussion

Meakin *et al.*[2,3] reported the $ED_{95}$ for atracurium to be 155 or 163 $\mu$g/kg from a dose-response study of infants. Our patient may have received 80 times the $ED_{95}$ over the half-hour period on this basis. There was no apparent disturbance to the child and full recovery of neuromuscular blockade appeared to be complete after 2.25 hours.

A.J. Charlton, FFARCS, N.J.N. Harper, FFARCS, Consultant Anaesthetists, D. Edwards, A.C. Wilson, Research Assistants, Department of Anaesthesia, Manchester Royal Infirmary, and St Mary's Hospital, Manchester M13 9WL.

Accepted 22 December 1988.

0003–2409/89/060485 + 02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

The metabolite laudanosine has been shown to cause seizure activity in animals, but this was not seen in our patient. Extrapolation from our two plasma values indicates that the concentration at the time of recovery of neuromuscular function was about 19 μg/ml, higher than the 17 μg/ml threshold required to produce seizures in dogs.[4] However, early seizure activity may have been masked by the neuromuscular blockade, although the seizure threshold has not been established in man.

Overdose of atracurium has been reported in a 3.9-kg neonate who received a 5.1-mg/kg bolus into a central vein.[5] Systemic hypotension and bronchospasm occurred, believed to be due to histamine release. The slow rate of injection in our patient may have prevented or limited histamine release,[6] and skin flushing, the only sign we observed, has been shown to occur without elevation of plasma histamine levels.[7]

We speculate that the consequences of such an accident with other non-depolarising relaxants would have been more serious and this apparent lack of toxicity in overdosage can be added to the list of advantages of atracurium.

## Acknowledgment

The authors thank Dr B. J. Pollard and the Wellcome Foundation for their assistance in making the HPLC facility available.

## References

1. Simmonds RJ. Determination of atracurium, laudanosine and related compounds in plasma by high-performance liquid chromatography. *Journal of Chromatography* 1985; **343:** 431–6.
2. Meakin G, Shaw EA, Baker RD, Morris P. Comparison of atracurium-induced neuromuscular blockade in neonates, infants and children. Proceedings of the Anaesthetic Research Society. *British Journal of Anaesthesia* 1987; **59:** 653P
3. Meakin G, Shaw EA, Baker RD, Morris P. Comparison of atracurium-induced neuromuscular blockade in neonates, infants and children. *British Journal of Anaesthesia* 1988; **60:** 171–5.
4. Chapple DJ, Miller AA, Wheatley PL. Neurological and cardiovascular effects of laudanosine in conscious and anaesthetised dogs. *Anesthesiology* 1985; **63:** A311.
5. Durcan J, Carter JA, Overdose of atracurium. *Anaesthesia* 1986; **41:** 767.
6. Scott RPF, Savarese JJ, Basta SJ, Embree P, Ali HH, Sunder N, Hoaglin DC. Clinical pharmacology of atracurium given in high dose. *British Journal of Anaesthesia* 1986; **58:** 834–8.
7. Barnes PK, de Renzy-Martin N, Thomas VJE, Watkins J. Plasma histamine levels following atracurium. *Anaesthesia* 1986; **41:** 821–4.

*Anaesthesia*, 1989, Volume 44, pages 487–489

CASE REPORT

# Paraplegia after coeliac plexus block

M. J. WOODHAM AND M. H. HANNA

## Summary

*A case is described in which paraplegia followed a coeliac plexus block performed using 90% alcohol under X ray screening. The likely cause was an ischaemic injury to the cord secondary to damage to the artery of Adamkiewicz. This rare complication seems difficult to avoid.*

## Key words

*Anaesthetic techniques, regional*; coeliac plexus block.
*Complications*; paraplegia.

Coeliac plexus block is a widely used technique for the control of upper abdominal visceral pain secondary to malignant disease.[1] Classically it has been indicated for the treatment of pain secondary to carcinoma of the pancreas, although it has been used in patients with chronic pancreatitis A hundred patients have been treated with coeliac plexus blockade in this centre over the last 4 years and the indications for this procedure are listed in Table 1. This table shows that a large number of our patients have either primary or secondary carcinoma of the liver, which reflects our pattern of patient referral. There had been no serious side effects until the case that is reported here.

**Table 1.** Indications for coeliac plexus block in the last 100 patients in this unit.

| | |
|---|---|
| Liver metastases | = 40% |
| Hepatoma | = 16% |
| Chronic pancreatitis | = 13% |
| Carcinoma pancreas | = 12% |
| Others | = 19% |

## Case history

Three months before referral to the pain relief unit the patient, a 62-year-old woman, was diagnosed as having disseminated carcinomatosis. She presented with complaints of abdominal pain, nausea, general malaise and occasional headaches. Her liver function tests were abnormal and a liver biopsy was performed; the histology showed 'infiltrating adenocarcinoma with dense surrounding fibrous tissue consistent with metastatic tumour'. This was treated by inserting an hepatic artery portacath at laparotomy followed by a course of 5-fluorouracil. The patient was then discharged and readmitted 3 months later.

She complained of worsening pain after re-admission and was referred to the pain relief unit. Her main complaint was of right upper-quadrant pain which radiated to her epigastrium. This was due to further enlargement of the liver metastases. She was taking regular paracetamol at that time but this was not controlling the pain and she was unwilling to take stronger analgesics. It was decided, after discussion with the patient, to proceed with a coeliac plexus block; the procedure was explained and formal consent obtained.

The technique used in this centre is similar to that described by Thompson.[1] The patient was starved on the morning of the procedure; no premedication was given. On arrival in the X ray department she was placed prone, an intravenous cannula inserted and an infusion of compound sodium lactate solution started. Sedation was achieved with midazolam and alfentanil. Local anaesthetic was infiltrated into the skin 8 cm lateral to the first lumbar vertebra bilaterally, and the two needles were then advanced at an angle of 45° to the skin, towards the midline, to strike the first lumbar vertebra. This was verified by X ray screening. The needles were then withdrawn before they were advanced at a more acute angle to the skin, with a slight cephalad angulation, testing for 'loss of resistance' continuously. The positions of the two needles were then checked with anteroposterior (AP) and lateral screening, when they were seen to lie 1.5 cm anterior and slightly lateral to the cephalic end of the first lumbar vertebra. The positions of the needles were

---

M.J. Woodham, FFARCS, Research Fellow, M.H. Hanna, FFARCS, Consultant, Pain Relief Unit, King's College Hospital, Denmark Hill, London SE5.
Correspondence should be addressed to Dr Hanna please.

Accepted 6 December 1988.

0003–2409/89/060487 + 03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

satisfactory and a 2-ml dose of radio-opaque dye (omnipaque 240) was injected down both needles consecutively.The spread on the left was satisfactory and conformed to the classical picture; however, on the right the spread of dye did not conform to the classical picture. It was decided to inject 90% alcohol 30 ml on the left and 0.25% bupivacaine 20 ml on the right. It is our normal practice to prevent hypotension prophylactically; therefore ephedrine 3 mg was given intravenously and a further 15 mg intramuscularly at the same time as the injection of alcohol. There were no significant changes in either arterial blood pressure or pulse rate during the procedure or after the blockade.

The patient was transferred back to the ward, and at this point she was still drowsy but responding to commands. Three hours later, she complained of numbness and weakness of her legs. A full neurological assessement showed minimal power in the legs with a total flaccid paralysis, except for a flicker of movement in the left second toe. There was a sensory level to pain, vibration and temperature at $T_{11/12}$, but there was partial preservation of sensation to light touch and a proportion of stimuli were sensed, in particular over the sacral dermatomes. The epigastric pain was relieved after the procedure.

A myelogram performed the next day was normal. A presumptive diagnosis of ischaemia of the cord secondary to damage to the artery of Adamkiewicz was made. There was minimal change in the patient's neurological condition in the 2 weeks after the procedure, and on her discharge she had no bladder control and minimal muscle power in her legs. She returned to the West Indies and died 2 months later.

## Discussion

The vascular supply of the spinal cord was first studied in 1882 by Adamkiewicz, and it was he who first described the arteria radicularis magna of Adamkiewicz (the largest of the anterior medullary feeders for the supply of the lumbar spinal cord). This area has since been studied further by other workers, and the artery of Adamkiewicz is known to have a variable entry site to the spinal cord; thus it may occur at any level between $T_7$ and $L_4$ although it is usually found at $T_9$ to $T_{11}$.[2,3] The artery of Adamkiewicz occurs on the left in 80% of cases. It is interesting, and may be relevant, that alcohol was only injected on the left in this patient.

The artery of Adamkiewicz is generally held to be important, but in some animal studies it has been ligated without any subsequent neurological consequences. There is a degree of variation between patients as to the number of anterior feeder arteries. This may vary from two to 17, although there are rarely more than nine.[3] Obviously the greater the number of other anterior medullary feeders the less critical will be the damage to the artery of Adamkiewicz. It may be that in older patients with a degree of arteriosclerosis the system of collaterals is compromised, thus increasing the importance of this artery.

Direct injection of alcohol into the cerebrospinal fluid (CSF) was considered extremely unlikely, since lateral and AP X ray screening was used and there were no neurological signs above $T_{11}$ after the procedure. Had alcohol been injected directly into the CSF then some spread of alcohol cephalad to the site of injection would be expected. It is also unlikely that alcohol was injected directly into the artery of Adamkiewicz, since no blood was aspirated before injection, and on screening one would expect rapid disappearance of the dye if the needle was situated in the artery itself.

The neurological damage in this case was probably due to spasm of the artery of Adamkiewicz in response to irritation caused by alcohol injected in close proximity to it, or mechanical damage by one of the needles, most probably the one sited on the left.

There have been three previous case reports of neurological lesions after coeliac plexus blockade.[4–6] Galizia and Lahiri in 1974[4] reported a case that involved the use of phenol which led to complete paraplegia, with a sensory level at $T_{12}$. X ray screening in this case was not used and there was a rapid onset of leg weakness at the time of injection. This was postulated to be secondary to an ischaemic injury to the spinal cord, but the most likely cause was damage to the artery of Adamkiewicz. Thompson in 1977[5] reported on a series of 100 coeliac plexus blocks which included one case of partial leg paralysis. This procedure was performed without the use of X ray screening and in the lateral position. The most likely cause of this neurological lesion was believed to be direct irritation of the lumbar nerve roots by alcohol.

The last and most recent case report that involved neurological damage after coeliac plexus block was by Cherry and Lamberty in 1984.[6] This again resulted in paraplegia with a sensory level at $T_{11-12}$. The sensory loss was variable whereas the motor deficit was profound. X ray screening was used in this last case, and once again the postulated cause of the neurological lesion was ischaemia of the cord secondary to damage (or spasm) of the artery of Adamkewicz. There was a period in this patient of 2–3 hours after the procedure before the onset of weakness and numbness. The patient received a general anaesthetic and the procedure was performed with the patient in the right lateral position.

It seems that there have been two previous case reports of ischaemic cord damage after injury to the artery of Adamkiewicz. It is difficult to say if the damage to the artery is secondary to injection of alcohol (or phenol) leading to spasm, or direct trauma by the needles used. X ray screening does not seem to reduce the chances of this occurring. The syndrome that is seen after injury to the artery of Adamkiewicz has certain characteristics, in particular dense motor weakness and variable sensory deficit, with a level around $T_{11-12}$.

This adverse complication of coeliac plexus block is fortunately rare and there have been few reported cases in the literature. It may happen in the hands of the most experienced of operators, and cannot be prevented by the use of X ray screening, or probably even the use of a CAT scanner. It could however be postulated that a coeliac plexus block performed using one needle on the right might be as effective as the bilateral approach and avoid this rare but serious complication.

## Acknowledgments

The authors thank Sister J. Latham and Dr S. Peat for their help with the preparation of this manuscript.

## References

1. Thompson GE. Celiac plexus, intercostal and minor peripheral blockade. In: Cousins MJ, Bridenbaugh PO, eds. *Neural blockade in clinical anaesthesia and management of pain.* Philadelphia: Lippincott, 1980: 384–404.
2. Guttmann L. Anatomical data on vertebral column and spinal cord. In: Gutmann L. *Spinal cord injuries: comprehensive management and research.* Oxford: Blackwell Scientific, 1973: 47–70.
3. Dommisse GF. The arteries, arterioles, and capillaries of the spinal cord: surgical guidelines in the prevention of postoperative paraplegia. *Annals of the Royal College of Surgeons of England* 1980; **62:** 369–76.
4. Galizia EJ, Lahiri SK. Paraplegia following coeliac plexus block with phenol. Case report. *British Journal of Anaesthesia.* 1974; **46:** 539–40.
5. Thompson GE, Moore DC, Bridenbaugh LD, Artin RY. Abdominal pain and alcohol celiac plexus block. *Anesthesia and Analgesia* 1977; **56:** 1–5.
6. Cherry DA, Lamberty J. Paraplegia following coeliac plexus block. *Anaesthesia and Intensive Care* 1984; **12:** 59–61.

*Anaesthesia*, 1989, Volume 44, pages 490–491

CASE REPORT

# The management of Caesarean section in a patient with an intracranial arteriovenous malformation

J. A. LAIDLER, I. J. JACKSON AND N. REDFERN

## Summary

*The anaesthetic management of elective Caesarean section in a 25-year-old woman with an inoperable intracranial arteriovenous malformation is described. The literature is reviewed.*

## Key words

*Anaesthetic techniques, regional*; epidural.
*Complications*; cerebral arteriovenous malformations, subarachnoid haemorrhage.

Subarachnoid haemorrhage is an uncommon obstetric complication that occurs in fewer than 1 in 10 000 pregnancies.[1] Maternal mortality has been reported to be as high as 80% with this condition, though this may have improved with current medical and surgical treatment.[1] We report here the management of Caesarean section in a patient with an inoperable intracranial arteriovenous malformation under epidural anaesthesia.

## Case history

A 25-year-old primigravid patient was admitted to hospital with a subarachnoid haemorrhage and was found to be 11 weeks pregnant. During the period of bed rest, she suffered greatly from nausea and vomiting and a further subarachnoid haemorrhage occurred. She was known to suffer from angiomatosis retinae and at the age of 21 years was found to have an arteriovenous malformation in the suprasellar region which was not thought to be amenable to surgery.

The patient made a full recovery and after discussion about the risks involved, elected to continue with the pregnancy. A further subarachnoid haemorrhage occurred at 24 weeks' gestation that required hospital admission, and at 34 weeks' gestation she was re-admitted for bed rest as a result of headaches and vomiting. She then remained in hospital until 38 weeks' gestation when an elective Caesarean section was performed She was normotensive throughout her pregnancy.

Epidural anaesthesia was selected. The mother was premedicated with ranitidine 150 mg orally 2 hours before surgery. Noninvasive arterial blood pressure and EEG monitoring were established. Intravenous access was secured and then the left radial artery was cannulated under local anaesthesia to allow direct arterial pressure monitoring. The mother's circulation was preloaded with 1 litre of plasma protein fraction (PPF) whilst an epidural was inserted at the $L_{2-3}$ interspace, with the patient lying in the left lateral position. The epidural was established after a test dose of 0.5% plain bupivacaine 3 ml, using further small increments of 0.5% plain bupivacaine. The arterial blood pressure was continuously monitored whilst a total of 25 ml of local anaesthetic was given over a period of 25 minutes. The Caesarean section was started when the block was confirmed to be above $T_5$ bilaterally. A further 500 ml of PPF was administered during surgery. A brief period of asymptomatic hypotension (systolic pressure 90 mmHg for less than 2 minutes) responded rapidly to a single dose of ephedrine 6 mg. Five units of syntocinon were administered after delivery of a healthy male infant, and a further 15 units were added to the intravenous infusion. Tubal ligation was performed as part of the procedure.

Monitoring was continued on the labour ward for 24 hours after operation. Analgesia was provided intravenously by a patient-controlled analgesia apparatus (Graseby PCAS) that delivered morphine and droperidol. She remained comfortable with a stable arterial blood pressure and suffered no nausea. Her recovery was uneventful and she was discharged from hospital one week after operation. Postnatal review at 6 weeks found her asymptomatic.

## Discussion

Subarachnoid haemorrhage is a rare complication of

---

J.A. Laidler, FFARCS, Registrar, I.J. Jackson, FFARCS, Senior Registrar, N. Redfern, FFARCS, Consultant, Newcastle General Hospital, Newcastle Upon Tyne.

Accepted 28 November 1988.

0003–2409/89/060490 + 02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

pregnancy and the puerperium. The overall incidence is variously quoted from 1 in 2000 to 1 in 10 000 pregnancies.[2] Pregnant women who suffer a subarachnoid haemorrhage are more likely to have an angiographically demonstrable lesion,[3] with arteriovenous malformations and aneurysms occurring with equal incidence. There are a number of factors which differentiate patients who bleed from an arteriovenous malformation from those who bleed from an aneurysm. Patients with the former tend to be younger (20–25 years), and are usually primiparous; bleeding is commonest at 15–20 weeks' gestation, but may occur at any stage including during labour or in the puerperium. The pregnant patient with such a malformation is more likely to suffer subarachnoid haemorrhage than her nonpregnant counterpart, and is also likely to suffer recurrent haemorrhage during the pregnancy.[4]

Patients with aneurysms, in contrast, tend to be older (30–35 years) and have had previous children without cerebral incident. They have an increasing risk of haemorrhage as the pregnancy progresses; the highest incidence is between 30 and 40 weeks' gestation. Surprisingly, it is rare for aneurysms to rupture during labour; however subarachnoid haemorrhage secondary to an aneurysm is more likely to be fatal. The outcome for the baby also differs between the two groups. In those with arteriovenous malformations the prognosis is below average in the first pregnancy and becomes worse in subsequent pregnancies if the arteriovenous malformation is untreated. The prognosis for the baby is poor if the mother is untreated, in the case of aneurysms, but normal if the mother has the aneurysm treated surgically.[3–5]

The neurosurgical management of these patients should be the same as in nonpregnant patients since this offers the best outcome for both mother and baby.[3] This means that early investigation and treatment should be carried out, if feasible. Clipping of aneurysms in the middle trimester has been followed by successful term delivery of healthy infants.[3–5] Peroperative maternal hypothermia appears to be well tolerated by the fetus, but the use of hypotensive techniques is more controversial.[3,5] Recent publications suggest that the fetus is unaffected by hypotension induced by the careful use of volatile anaesthetics, beta-adrenoceptor-blockers or sodium nitroprusside,[5,6] although maternal placental perfusion and therefore fetal oxygenation is directly related to mean arterial pressure. Aneurysmal clipping immediately after Caesarean section has also been reported with a successful outcome.[7] Conservative management of patients with aneurysms carries a worse prognosis than finding an inoperable arteriovenous malformation. The obstetric management of both groups of patients after surgical treatment is vaginal delivery at term where possible. The use of epidural analgesia, forceps to assist delivery and careful administration of oxytocics has been recommended.[3] It is considered that the risk of recurrent haemorrhage from an untreated malformation makes delivery by elective Caesarean section at 38 weeks' gestation mandatory.[3–5] The deleterious effects of pregnancy on arteriovenous malformations and the increased risk of haemorrhage with further pregnancies makes sterilisation of the patient advisable.

The choice of anaesthetic technique for Caesarean section in these patients is influenced by the need to maintain a stable cardiovascular system.[8] The preference for epidural anaesthesia in this case was influenced by the desire to avoid the hypertensive response to tracheal intubation and the narcotics necessary to modify this. Epidural anaesthesia, utilising small increments of local anaesthetic to give the gradual onset of sympathetic blockade accompanied by adequate circulatory preload, and the use of small doses of ephedrine as required provides the necessary cardiovascular stability. It is important to avoid hypotension, which may occur as an epidural block becomes established, since this may induce nausea and even vomiting. The increase in intracranial pressure caused by vomiting can be dangerous; indeed this patient suffered two of her subarachnoid haemorrhages in association with the morning sickness of early pregnancy.

Postoperative analgesia must be effective and again should not compromise cardiovascular stability. The risk of nausea and vomiting should be minimised and respiratory depression avoided. Epidural analgesia using local anaesthetic boluses, infusions or even epidural opioids may be utilised. Patient-controlled analgesia is another technique that is being used increasingly for postoperative pain relief. This technique is routinely provided for mothers who undergo Caesarean section in our unit. This technique, in our experience, provides good quality analgesia with a low incidence of nausea and hence it was used in this case.

## References

1. Reece EA, Chervenak FA, Coultrip L, Hobbins JC. The perinatal management of pregnancy complicated by massive intracerebral hemorrhage. *American Journal of Perinatology* 1984; **1:** 266–7.
2. Nedd KJ, Kent M, Powell V. Subarachnoid hemorrhage during pregnancy and the puerperium: report of 3 cases and review of the literature. *Journal of the American Osteopathic Association* 1986; **86:** 183–8.
3. Robinson JL, Hall CJ, Sedzimir CB. Subarachnoid hemorrhage in pregnancy. *Journal of Neurosurgery* 1972; **36:** 27–33.
4. Robinson JL, Hall CS, Sedzimir CB. Arteriovenous malformations, aneurysms, and pregnancy. *Journal of Neurosurgery* 1974; **41:** 63–70.
5. Tuttelman RM, Gleicher N. Central nervous system hemorrhage complicating pregnancy. *Obstetrics and Gynecology* 1981; **58:** 651–6.
6. Willoughby JS. Sodium nitroprusside, pregnancy and multiple intracranial aneurysms. *Anaesthesia and Intensive Care* 1984; **12:** 351–7.
7. Conklin KA, Herr G, Fung D. Anaesthesia for caesarean section and cerebral aneurysm clipping. *Canadian Anaesthetists' Society Journal* 1984; **31:** 451–4.
8. Milsom I, Forssman L, Biber B, Dottori O, Rydgren B, Sivertsson R. Maternal haemodynamic changes during caesarean section: a comparison of epidural and general anaesthesia. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 161–7.

*Anaesthesia*, 1989, Volume 44, pages 492–493

CASE REPORT

# Failure of repeated blood patch in the treatment of spinal headache

R. A. FRY AND A. PERERA

## Summary

*The management of a persistent, incapacitating postdural puncture headache that required four consecutive autologous epidural blood patches is presented. Inadequate blood volumes, early patching and steroid in the epidural space are considered as possible causes of failure. Other associated problems and interventions are briefly discussed.*

## Key words

*Complications*; headache.
*Anaesthetic techniques, epidural*; blood patch.

The treatment of postdural puncture headache remains controversial. An epidural blood patch administered 24 hours after the dural puncture is one of the advocated methods of treatment.[1] We report here a 37-year-old woman with an $L_5$-$S_1$ intervertebral disc protrusion who was treated with epidural steroid injections for sciatic pain, and received an inadvertent spinal tap that resulted in a postdural puncture headache which proved extremely difficult to treat.

## Case history

A 37-year-old woman was referred to the pain clinic from a peripheral hospital for the management of low back pain and right-sided sciatica. She was rather obese and of short stature and had CT evidence of $L_5$-$S_1$ disc prolapse. A lumbar epidural injection had been performed 4 weeks earlier, during which time an unrecognised dural puncture occurred that resulted in an occipital headache 8 hours later. The headache resolved in a few days on bed rest alone.

A second epidural using Depo-Medrone 80 mg in 5 ml of 0.5% lignocaine made up to a volume of 20 ml with normal saline was uneventful and afforded good pain relief. Four weeks later the patient re-attended with complaints of severe backache; she had injured it mowing the lawn. A definite cerebrospinal fluid (CSF) leak was noted when an epidural was performed at the $L_{4-5}$ interspace with an 18-gauge Tuohy needle and a severe headache and lightheaded feeling was reported by the patient.

Ten millilitres of autologous blood was immediately administered into the epidural space at $L_5$-$S_1$ after injection of the steroid and local anaesthetic. The patient indicated some relief from this intervention but about an hour later the headache returned. She was admitted to hospital and a further blood patch performed 10 hours postpuncture, using 15 ml of autologous blood injected at the $L_{3-4}$ interspace. The headache again resolved but despite complete bed rest returned with the same intensity a few hours later.

The patient requested to be discharged home despite the persistent headache and returned on day five postdural puncture, somewhat dehydrated, still complaining of occipitofrontal headache, nausea, meningism and photophobia. Her admission temperature was 36.5°C. A third epidural blood patch was performed at $L_{4-5}$ using 15 ml autologous blood after instituting intravenous fluid therapy and an epidural catheter was left *in situ*. Total relief from headache again ensued but lasted only 2 hours. A saline infusion into the epidural space was soon discontinued since the catheter was found to have been accidentally displaced.

Narcotic pain relief was withheld until this time due to alleged previous allergic reactions to morphine and pethidine. The patient was already taking a mixture of naproxen and dextropropoxyphene for her backache, together with aspirin and paracetamol when required. Administration of papaveretum intramuscularly however caused no reaction and produced a degree of pain relief.

An intravenous infusion, on the seventh day after dural puncture, of caffeine sodium benzoate 500 mg in one litre of lactated Ringer's solution given over an hour and

---

R.A. Fry, MB, ChB, Registrar, A. Perera, FFARCS, FFARACS, Consultant, Pain Clinic, Northland Base Hospital, P.O. Box 743, Whangerei, New Zealand.
Correspondence should be addressed to Dr R.A. Fry, Anaesthetic Department, Frenchay Hospital, Bristol BS16 1LE.
Accepted 11 November 1988.

0003–2409/89/060492 + 02 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

followed by one litre of 5% dextrose in saline resulted in severe nausea and vomiting. However, a fourth blood patch performed concurrently at the $L_{4-5}$ interspace using 20 ml of autologous blood finally relieved the headache and photophobia completely.

### Discussion

A recent literature survey revealed that this case appears to be the only reported dural puncture that required more than two epidural blood patches, apart from one in which three deliberate dural punctures were performed during administration of blood patches.[2] Several possible causes for the initial failure of the technique are considered.

Postdural puncture headaches often have a delayed onset in patients in hospital but under outpatient conditions they often occur soon after the dura is penetrated. The duration of symptoms in the untreated patient varies from a few days to more than a year. Complete recovery, in general, usually occurs within a week, as demonstrated in this patient after the initial dural puncture.[3] It is now recommended that epidural blood patches are performed approximately 24 hours after puncture; their efficacy decreases with earlier administration.[4] This is impractical in the outpatient situation and hence a blood patch was performed immediately. This may have been a factor that favoured failure in the first two attempts, although a recent report indicates the critical factor involved is adequate volume rather than the timing of the blood patch.[5]

Volumes of autologous blood between 10 and 20 ml have been advised in the past but a higher success rate is reported using the latter.[6,7] The volumes utilised in the three unsuccessful blood patches were all less than 20 ml, which was the volume which finally succeeded. Controversy also exists about the correct intervertebral space to utilise for the technique. In general, due to greater cephalad spread, the same level as the puncture or one space below if the former is not possible, appears most accepted.[1,3] These recommendations were followed in all but one of the epidural blood patches performed in this case. The aspiration of CSF at the time of patching has been implicated in failure, but none was noted during any of the four attempts.[1]

The possibility of a clotting abnormality was not completely excluded since a bleeding time requested was not performed before discharge. However, despite her medications the patient demonstrated a hypercoagulable state: prothrombin clotting time 16 seconds (control 13 seconds), thrombin clotting time 7 seconds (control 9 seconds), activated prothrombin time 28 seconds (control 33 seconds) and a platelet count of 470 × $10^9$/litre. A local steroidal effect within the epidural space could possibly have interfered with the success of the blood patch, either because of the dilution effect from the volume of injectate or due to a direct interaction with blood clotting mechanisms.

Saline infusion into the epidural space was abandoned because of catheter displacement but has been utilised successfully to treat postspinal headaches, and further patching via the catheter, although considered, was finally unnecessary.[8–10]

First line therapy for spinal headaches often includes analgesic drugs, although indomethacin has recently been shown to have no significant effect in such situations.[11] The patient was already utilising a multitude of medications and indicated two previous allergic reactions to pethidine and morphine.

Further medication was therefore withheld until later in her treatment. Caffeine sodium benzoate was also instituted late but abandoned due to its side effects; it has recently been advocated as a first-line intervention in spite of a success rate of around 70% even with the second dose.[12,13]

Most patients with spinal headache are permanently relieved of their symptoms after a single epidural blood patch; a success rate that approaches 100% is achieved after a second should the initial one fail. Occasionally, as illustrated by this case, exceptions occur which can cause undue stress to both patient and physician. Delayed blood patching, although difficult in an outpatient may prevent unnecessary failure even though immediate prophylaxis is still advocated as a useful technique.[14] Certainly larger volumes of blood appear universally to produce better results. This case reinforces the occasional need to persist with repeated blood patches to achieve a permanent cure.

### Acknowledgment

The authors acknowledge the assistance of Mrs L. Hewitt, Medical Typist, in the preparation of this manuscript.

### References

1. BROWNRIDGE P. The management of headache following accidental dural puncture in obstetric patients. *Anaesthesia and Intensive Care* 1983; **11:** 4–15.
2. CASEMENT BA, DANIELSON DR. The epidural blood patch: are more than two ever necessary? *Anesthesia and Analgesia* 1984; **63:** 1033–5.
3. OLSEN KS. Epidural blood patch in the treatment of post lumbar puncture headache. *Pain* 1987; **3:** 293–301.
4. LOESER EA, HILL GE, BENNETT GM, SEDEBERG JH. Time vs success rate for epidural blood patch. *Anesthesiology* 1978; **49:** 147–8.
5. CHEEK TG, BANNER R, SAUTER J, GUTSCHE BB. Prophylactic epidural blood patch is effective. A preliminary communication. *British Journal of Anaesthesia* 1988; **61:** 340–2.
6. CRAWFORD JS. Headache after lumbar puncture. *Lancet* 1981; **ii:** 418.
7. CRAWFORD JS. Experiences with epidural blood patch. *Anaesthesia* 1985; **40:** 381.
8. CRAWFORD JS. The prevention of headache consequent upon dural puncture. *British Journal of Anaesthesia* 1972; **44:** 598–600.
9. STEVENS RA, JORGENSEN N. Successful treatment of dural puncture headache with epidural saline infusion after failure of epidural blood patch. Case report. *Acta Anaesthesiologica Scandinavica* 1988; **32:** 429–31.
10. SHAH JL, VENESS AM. Epidural blood patch using a catheter. Diagnosis of an unrecognised dural tap. *Anaesthesia* 1985; **40:** 1120–3.
11. FLAATTEN H, RODT S, ROSLAND J, VAMNES J. Postoperative headache in young patients after spinal anaesthesia. *Anaesthesia* 1987; **42:** 202–5.
12. BAUMGARTEN PK. Should caffeine become the first line treatment for post dural puncture headache? *Anesthesia and Analgesia* 1987; **66:** 913–4.
13. JARVIS AP, GREENAWALT JW, FAGRAEUS L. Intravenous caffeine for post dural puncture headache. *Anesthesia and Analgesia* 1986; **65:** 316–7.
14. ACKERMAN WE, COLCOUGH GW. Prophylactic epidural blood patch: the controversy continues. *Anesthesia and Analgesia* 1987; **66:** 913.

*Anaesthesia*, 1989, Volume 44, pages 494–497

APPARATUS

# A new dual function nerve stimulator

A. J. SANSOME AND J. G. DE COURCY

## Summary

*The Duostim model TV02 is a new peripheral nerve stimulator designed both for nerve identification in the performance of regional anaesthesia and for monitoring neuromuscular blockade. The output pulses are unipolar and of adjustable constant current. The provision of single twitch (1 Hz and 1/15 Hz) train-of-four and tetanic stimuli, together with indication of the current delivered and the small size of the unit, facilitate its clinical use. Performance was assessed and found to be according to specification.*

## Key words

*Equipment*; nerve stimulator.
*Monitoring*; neuromuscular function.

The use of peripheral motor nerve stimulation to permit assessment of the degree of neuromuscular blockade has been advocated by many authors.[1–4] Similarly, use of low output nerve stimulators was recommended to facilitate the performance of regional anaesthetic procedures.[5–9]

Few nerve stimulators currently available in the UK are dedicated to performing both functions. A new device has been developed in response to this which combines both, with ease of portability and low cost (permitting ownership by the individual anaesthetist). It is portable, is intended for daily use as a neuromuscular monitor and is readily available aid for the performance of regional anaesthesia.

## Description

The Duostim Model TV02 is a peripheral nerve stimulator for use in anaesthetics. It is battery powered, and housed in a small black plastic case 118 mm × 32 mm × 66 mm with an integral PP3 battery compartment.

Its two principal functions, with separate outputs via a multipin connector, are for neuromuscular blockade monitoring and nerve identification. The output current control, on/off switch, mode and function switches, indicator lights and output connector are all mounted on the front panel (Fig. 1). The facilities are summarised below.

### *Neuromuscular blockade monitoring*

Design pulse: 200 μsec, square wave, 220 V maximum. Repetition rates: 50 Hz tetanic; 1 pulse per 15 seconds (for onset time); 1 Hz (for post-tetanic count); 2 Hz train-of-four (TOF);[1–10] single TOF; standby mode repeated every 1 or 2 minutes.

To facilitate the assessment of post-tetanic potentiation the device automatically delivers a TOF or a continuous 1 Hz after a tetanic burst according to the function selected.

### *Nerve identification*

Design pulse: 1 msec, square wave 16 V maximum. Repetition rates: all of the above functions are available with the exception of the 50 Hz tetanic stimulus, although the use of 1 Hz is recommended.

### *General features*

Audible and visual indications of output pulse generation are provided respectively by a piezo-electric transducer and a green light-emitting diode (LED). To warn the user of an impending TOF in the autorepeating standby mode, the unit produces a bleep two seconds before the delivery of the stimulus.

---

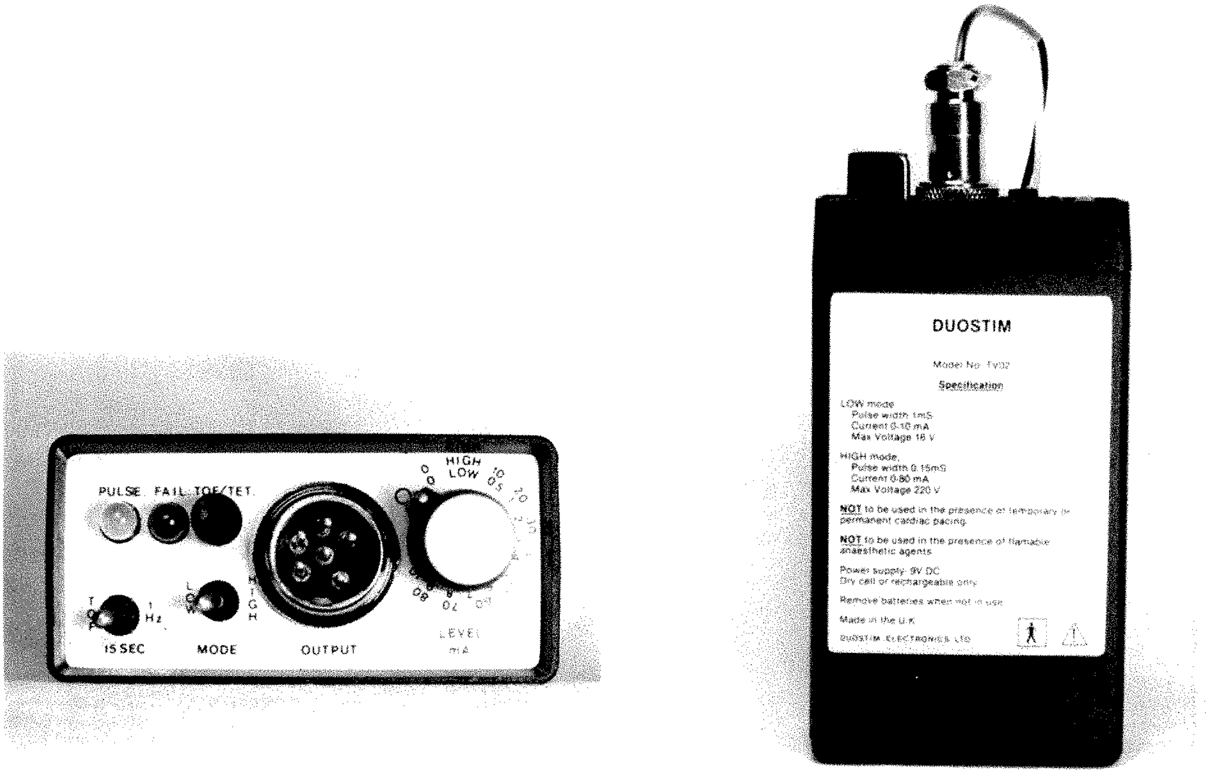
A.J. Sansome, MB, ChB, FFARCS, Senior Registrar, Shackleton Department of Anaesthetics, Southampton General Hospital, Tremona Road, Southampton, Hampshire SO9 4XY, J.G. de Courcy, MB, BS, DA (UK), DCH, Registrar, Department of Anaesthetics, Poole General Hospital, Longfleet Road, Poole, Dorset.

Correspondence should be addressed to Dr A.J. Sansome please.

Accepted 28 October 1988.

0003–2409/89/060494 + 04 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland



LOW mode
Pulse width 1mS
Current 0-10 mA
Max Voltage 16 V

HIGH mode,
Pulse width 0.15mS
Current 0-80 mA
Max Voltage 220 V

NOT to be used in the presence of temporary or permanent cardiac pacing.

NOT to be used in the presence of flammable anaesthetic agents

Power supply: 9V DC
Dry cell or rechargeable only

Remove batteries when not in use

Made in the U.K.

DUOSTIM ELECTRONICS LTD

Fig. 1. The Duostim peripheral nerve stimulator, controls and markings.

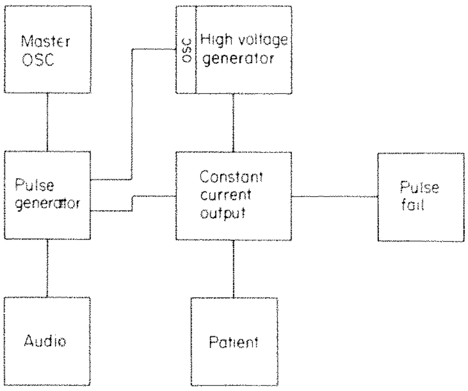


**Fig. 2.** Block diagram of the unit.

The unit acts as a constant current generator in both modes.[2,11] It delivers an operator-selected current which is independent of skin impedance within its normal range. The current during the output pulse is measured and compared with that set by the output level control. Should the output fail to achieve the preset current then a second red LED flashes to warn the user.

To avoid the accidental delivery of a high current during nerve identification, the two principal functions are performed using separate leads, which are colour coded and connect to different pins in the output connector. Should the lead and mode selected not match, no current will be delivered and the red warning LED will flash.

## Methods

The device was investigated to assess its output waveforms, timing accuracy and constant output current characteristics. The dependence of the timing and maximum output voltage on supply voltage variation was also investigated. The equipment used for this investigation consisted of a Grundig MO22-20 MHz dual-beam oscilloscope, a Thurlby PL310 stabilised power supply, a Sinclair DM235 digital multimeter, a capacitor of 47 nF (tolerance 5%) and resistors of 5, 100, 1 K, 10 K, and 100 K ohms (tolerance 1%).

The output waveforms in both modes were displayed on the oscilloscope: the unit drove a resistive load of 1 K ohm and a reactive load represented skin impedance (personal communication: Dr I. Swain, Odstock Hospital, Salisbury) of 1 K ohm in parallel with 47 nF capacitance. The current drawn from a 9 V supply was measured with the digital multimeter during both standby and 50 Hz-tetanic stimulation at a preset 50 mA output.

The supply voltage range over which the maximum specified output voltage could be maintained was determined, and the timing accuracy was checked at 9 V and at the lower limit of this range into a resistive load of 1 K ohm.

A blinded investigation of the constant output current characteristics was performed. The voltage generated across various loads was measured with the oscilloscope, and the current calculated from Ohm's law ($I = V/R$). One investigator unable to see the oscilloscope preset the desired output current while measurements were made by another.

## Results

A block diagram of the unit is shown in Figure 2. The output voltage and current into a resistive load in both modes are unidirectional square wave pulses whose amplitude is dependent on the preset output current. The output waveforms into a load of 1 K ohm in parallel with 47 nF are shown in Figure 3.

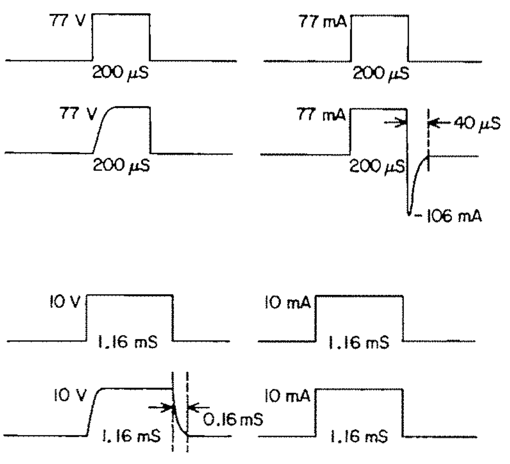


**Fig. 3.** Output waveforms. The top two in the HIGH mode (neuromuscular monitoring); the upper into a 1 K ohm load, the lower into 1 K ohm in parallel with 47 nF. The bottom two in the LOW mode (nerve identification); the upper into 1 K ohm, the lower into 1 K in parallel with 47 nF. In each case the first waveform depicts the output voltage, the second the current.

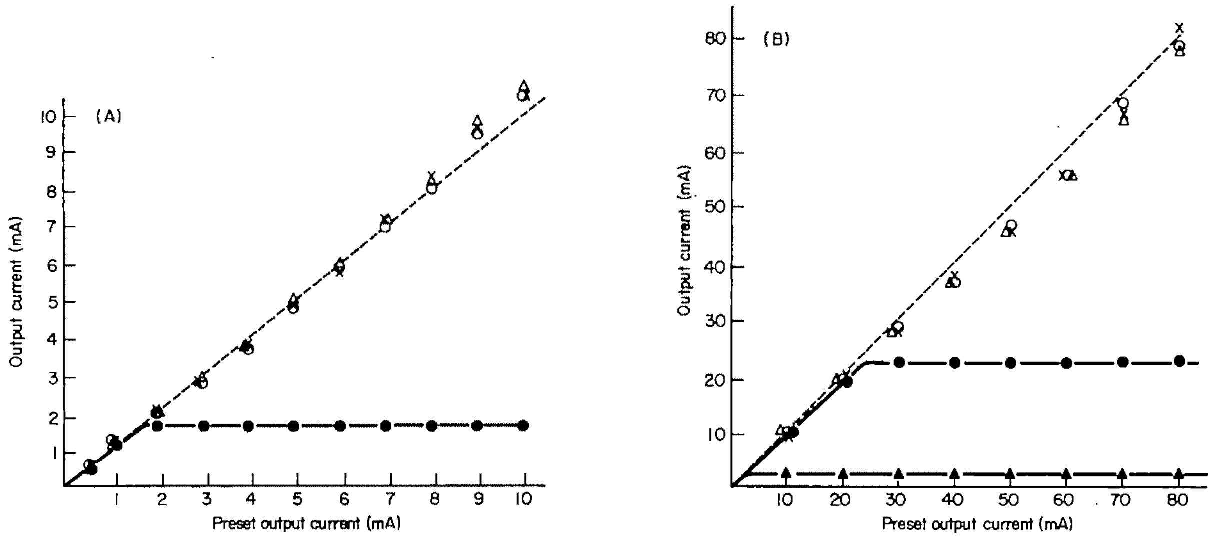


**Fig. 4.** Graphs (A) (LOW mode) and (B) (HIGH mode) display the relationship between the output current set and that flowing, for load resistances of 5 ohms, O; 100 ohms, Δ; K ohms, ×; K ohms × 10, ●; and in the high mode K ohms × 100, ▲. In each case the dashed line indicates equivalence. Note that if the load resistance is too high (O, ▲) the maximum current becomes limited by the maximum available output voltage.

The unit consumes 0.71 mA at 9 V in the standby mode, and during 50 Hz tetanic stimulation with an output current of 50 mA, it consumes 12 mA. This implies a long battery life, which has been confirmed by clinical experience. The relationship between the preset output current and that calculated from the measured voltages generated is displayed for a variety of load resistances (Fig. 4).

## Discussion

Several studies have advocated the use of peripheral nerve stimulation to facilitate the performance of regional anaesthesia and to reduce the risk of nerve damage associated with the search for paraesthesia.[5–7,12] The use of peripheral nerve stimulators in the monitoring of neuromuscular blockade has been widely recommended.[1–3] It has been shown that 40% of patients whose reversal has been judged on clinical grounds alone may subsequently exhibit evidence of neuromuscular block.[3] Furthermore, the use of neuromuscular monitoring facilitates the control of intra-operative relaxation, particularly with the shorter acting agents[13] and allows the dose of anticholinesterase to be adjusted to the patient's needs.[2]

The minimum requirements of a peripheral nerve stimulator for neuromuscular monitoring have been proposed in a recent review.[2] The authors recommend square wave pulses of 0.2 msec duration, repeated at 1 Hz, 2 Hz TOF and 50 Hz tetanic. They suggest that the current should be indicated and adjustable up to 35 mA. Others have advocated the use of constant current outputs (rather than constant voltage) of up to 60 mA.[14] These criteria appear to have been fulfilled by the device tested, with the additional features of 1/15 Hz, autorepeating TOF and audible indications of both an impending TOF and the delivery of the stimuli.

Stimuli repeated more frequently than once every 10 seconds are associated with a reduction in twitch tension, and therefore 0.1 Hz has been recommended as the maximum single twitch frequency.[1]

The calibration of the output level-control is sufficiently accurate for clinical use, as can be seen from Figure 4 and, in conjunction with the visual indication of failure to achieve the specified output, avoids the need for the current to be displayed.

A recent review[6] of the use of peripheral nerve stimulators in regional anaesthetic practice has recommended that these devices should have a constant current output with a level-control with a linear response, short output pulses (50 to 100 μsec) repeated at 1 Hz. The output current should be displayed (preferably digitally) and, if the device is to be used for neuromuscular monitoring and nerve identification, both high and low ranges should be available. Indication of low battery-voltage should be provided. The leads should have clearly marked polarity and be terminated with high quality alligator clips. Another author has suggested that output pulses of 1 msec duration, repeated at 1 Hz should be used with a stimulus current down to less than 0.5 mA.[15] The current failure-indicator LED and calibrated level-control make an output current display unnecessary.

In summary, the unit is a small dual-function peripheral nerve stimulator which provides a clinically useful range of features dedicated to both neuromuscular monitoring and nerve identification.

The Duostim Peripheral Nerve Stimulator is marketed by Medical Marketing, P.O. Box 37, Grantham, Lincolnshire, NG31 6AA. £74.64 including VAT.

## References

1. Ali HH, Savarese JJ. Monitoring neuromuscular function. *Anesthesiology* 1976; **45:** 216–49.
2. Hudes E, Lee KC. Clinical use of peripheral nerve stimulators in Anaesthesia. *Canadian Journal of Anaesthesia* 1987; **34:** 525–34.
3. Viby-Mogensen J, Jorgensen BC, Ording H. Train-of-four quantitation of residual neuromuscular blockade in the recovery room. *Anesthesiology* 1979; **50:** 539–41.
4. Norman J. Competitive neuromuscular blocking drugs. In: Kaufman L, ed. *Anaesthesia review 1.* Edinburgh, London, Melbourne, New York: Churchill Livingstone, 1982.
5. Raj PP. Ancillary measures to assure success. *Regional Anesthesia* 1980; **5:** 9–12.
6. Pither CE, Raj PP, Ford DJ. The use of peripheral nerve stimulators for regional anesthesia: a review of experimental characteristics, techniques and clinical applications. *Regional Anesthesia* 1985; **10:** 49–58.
7. Raj PP. Rosenblatt R, Montgomery SJ. Use of the nerve stimulator for peripheral nerve blocks. *Regional Anesthesia* 1980; **5:** 14–21.
8. Smith BE, Allison A. Use of a low power nerve stimulator during sciatic nerve block. *Anaesthesia* 1987; **42:** 296–8.
9. Raj PP. Mechanical Aids. In: Henderson JJ, Nimmo WS, eds. *Practical regional anaesthesia.* Oxford, London, Edinburgh, Boston, Melbourne: Blackwell Scientific Publications, 1983: 321–32.
10. Ali HH, Utting JE, Gray TE. Stimulus frequency in the detection of neuromuscular block in humans. *British Journal of Anaesthesia* 1970; **42:** 967.
11. Capan LM, Satyanarayana T, Patel KP, Turndorf H, Ramanathan S. Assessment of neuromuscular blockade with surface electrodes. *Anesthesia and Analgesia* 1981; **60:** 244–5.
12. Chapman GM. Regional nerve block with the aid of a nerve stimulator. *Anaesthesia* 1972; **27:** 185–93.
13. Feldman SA. Neuromuscular Block. In: Churchill-Davidson HC, ed. *A practice of anaesthesia.* London: Lloyd Luke, 1984: 676–707.
14. Kopman AF, Lawson D. Milliamperage requirements for supramaximal stimulation of the ulnar nerve with surface electrodes. *Anesthesiology* 1984; **61:** 83–85.
15. Galindo A. *Regional anaesthesia.* Miami: R.N. Scientific Publications, 1982.

*Anaesthesia*, 1989, Volume 44, pages 498–503

APPARATUS

# The Malawi anaesthetic machine

## Experience with a new type of anaesthetic apparatus for developing countries

P. M. FENTON

## Summary

*One year's experience with a new type of oxygen concentrator and anaesthetic machine, designed for anaesthesia in developing countries, is presented. The apparatus, its performance and problems are described and the author's suggested modifications to improve the original design are outlined. The apparatus, with these changes, represents a significant advance in oxygen availability for hospitals in developing countries as well as improving the anaesthetic capabilities.*

**Key words**

*Equipment*; anaesthetic machines, vaporizers.
*Oxygen*; delivery systems.

Anaesthetic equipment in developing countries is often old and broken and has connexions that are incompatible with modern 22-mm ISO[1] spare parts and accessories. In addition, equipment either donated by Western countries or else ordered by local misguided individuals may never be used because of incompatibility. The commonest example of this is in the author's experience, the Boyle's machine or ventilator that requires compressed gas or air to operate it where this facility is not available. The 'high tech' store room of useless machines is a familiar and well publicised feature of many Third World hospitals.

The concept has been proposed of an apparatus that can be adapted to give an anaesthetic under all the conditions that may prevail in a developing country, for example, from simple drawover with ether and air, to artificial ventilation with nitrous oxide–oxygen, and added volatile agent.[2]

In Malawi, Central Africa, in 1986, an anaesthetic machine made by Simonsen and Weel* was introduced which put part of this concept into practice. A domestic-use oxygen concentrator was adapted to supply oxygen and air via a pipeline to a unique combination of continuous flow/drawover anaesthetic machine. A continuous oxygen supply is thus on hand as long as electricity is available to power the concentrator.

This report is based on experience with its use in Southern Malawi between May 1987 and May 1988. The Southern Region of Malawi has seven out of 21 government district hospitals nationwide and two out of three central or general hospitals (loosely defined as centres where specialist care is available). Of the total population of Malawi, 49.6% inhabit the region, therefore theatre operating time would be expected to be above the national average.[3] The largest hospital in Malawi, holding some 1000 inpatients, is located in the region.

The region, though lower in altitude than some central and northern areas, is broadly representative of the varying climatic conditions of Malawi as a whole, with minimum temperatures of approximately 10°C in the highlands and maximum temperatures in the range 45–48°C in the lower Shire Valley. Extremes of humidity occur according to the season; however, most operating theatres have some form of air conditioning, operating albeit infrequently.

Thus the performance of this equipment in the region should be applicable to the country as a whole and to other developing countries with hot humid climates.

### The Malawi model anaesthetic machine

The apparatus comprises two separate units, the oxygen concentrator and the anaesthetic machine itself with its accessory equipment.

The concentrator, a De Vilbiss DeVo/44, 240 V AC, designed for domestic oxygen therapy has been modified by the addition of two push-release pipeline pressure coupling outlets for oxygen and compressed air. This concentrator works by pumping room air from a compressor through two canisters containing 'Xeolite' which absorbs nitrogen. The canisters are automatically switched alternately so that oxygen is available from one canister while the other

---

*S & W Medical Technology, Ruxley Corner, Sidcup, Kent DA14 5BL.

P.M. Fenton, DTM&H, FFARCSI, Anaesthetic Specialist, Queen Elizabeth Central Hospital, P.O. Pox 95, Blantyre, Malawi, Central Africa.

Accepted 4 November 1988.

0003–2409/89/060498 + 06 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

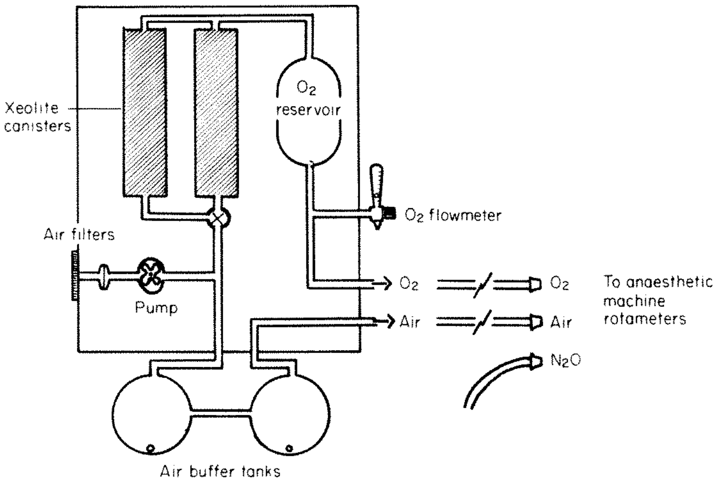


**Fig. 1.** Schematic diagram of oxygen concentrator.

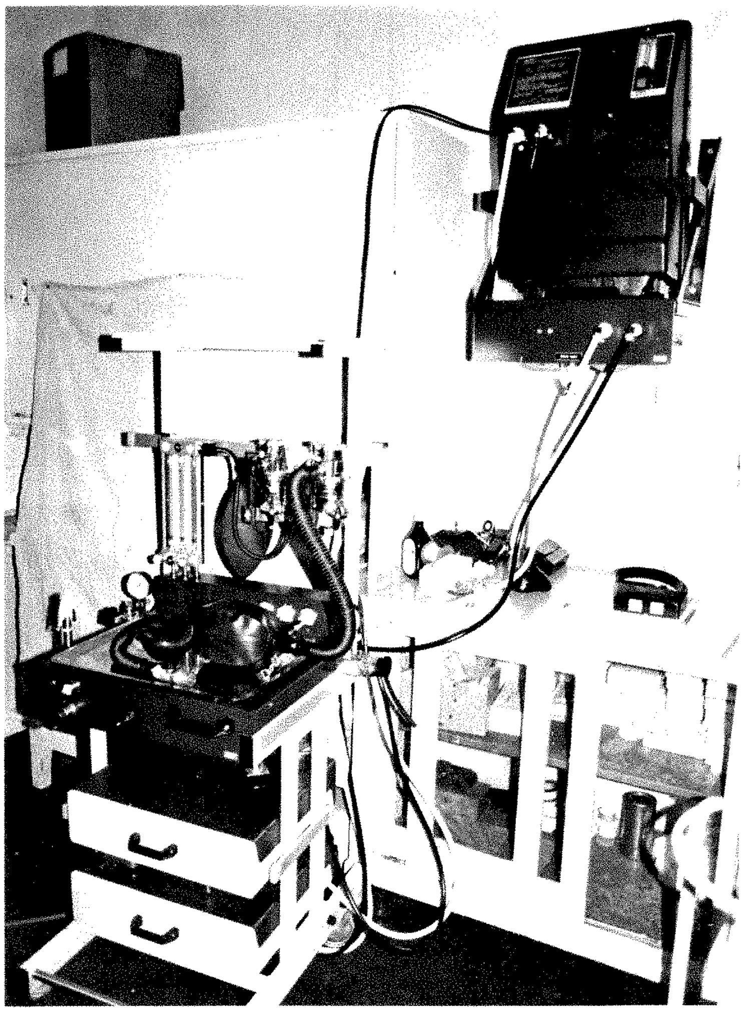


**Fig. 2.** The concentrator and anaesthetic machine.

is regenerated. The principle is common to most oxygen concentrators and is described elsewhere.[4]

The compressor not only pumps air to the Xeolite canisters but also supplies compressed air to the air outlet and thence to two pressurised buffer tanks. These serve to smooth over changes in air pipeline pressure which would otherwise occur during the canister switching process, and act as traps for condensed water vapour which can be drained at their bases. These tanks are integral with and form the base of a wall-mounted bracket that supports the concentrator unit proper, placed some 2 m from the ground (Fig. 1).

The original outlet for oxygen, a simple nipple with a flowmeter control up to 5 litres/minute, is retained as a separate oxygen source. This can be used for neonatal resuscitation and for ward connexions when the concentrator is lifted from its bracket, after disconnexion of the pipelines, and wheeled to where it is needed.

The compressor pump in the concentrator can generate a pressure of 180 kPa and is fitted with three alarms: for

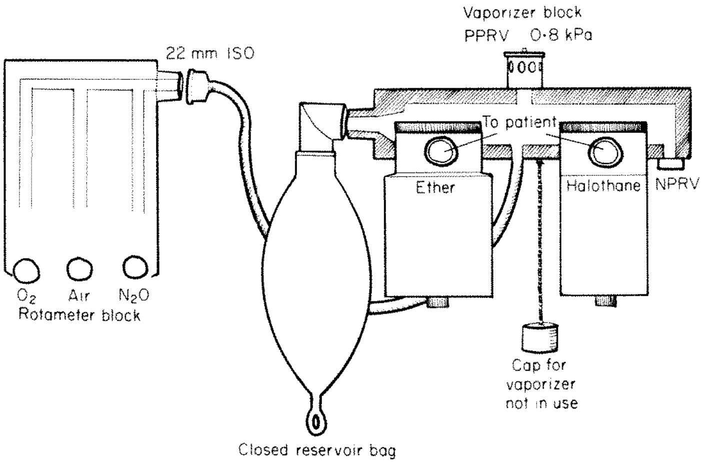


**Fig. 3.** Arrangement of Rotameters and vaporizers.

overpressure and underpressure and a blocked air intake filter.

The concentrator is connected to the anaesthetic machine by 5–6 m of pipeline hose for oxygen and air (Fig. 2). The machine has push-release noninterchangeable connectors at the rear for oxygen, air and nitrous oxide and these three gases are controlled by flowmeters as in a conventional Boyle's machine. A safety switch prevents simultaneous selection of air and nitrous oxide together.

A low pressure soft rubber pipe leads from a 22-mm ISO standard conical connector at the top of the Rotameter block, (where, in a conventional Boyle's machine the back-bar mounted vaporizer would be sited) to a detachable vaporizer block which has Ohmeda 'Tec' drawover vaporizers for ether and halothane mounted in parallel. The pressure in the Rotameter block could rise to 180 kPa therefore a positive pressure relief valve (PPRV) is provided on the vaporizer block. The opening pressure of this PPRV (nonadjustable) is high at 0.8 kPa. This valve also prevents jamming of the Ambu valve in the patient system.

The vaporizer block is freely movable between a fitted swivel mount at table-top level and the back bar and can be removed from the machine. The oxygen flush (oxygen from the concentrator) can only be used when the vaporizers are mounted on the swivel. The vaporizers are in parallel so only one can be used at a time: the one not in use is capped off (Fig. 3).

A reservoir bag is provided to monitor spontaneous breathing. The patient system leads from the selected vaporizer to an Ambu bag and Ambu inflating (nonrebreathing) valve so that positive pressure ventilation may be given as required (Fig. 4).

This arrangement of vaporizer, self-inflating bag and inflating valve is the same as other drawover systems such as the EMO or Triservice apparatus. The closed reservoir bag on the vaporizer block replaces the conventional open-ended oxygen reservoir tube of the EMO or Triservice drawover systems: if the fresh gas flow from the Rotameter block exceeds the patient's requirements the bag fills and when full, the excess vents via the PPRV.

The pressure in the patient system will increase to 0.8 kPa in the event of a pause in breathing by the patient or during any other outflow obstruction at the inflating valve. This contrasts sharply with conventional drawover systems where pressure in the system is always atmospheric. Air is entrained via a small negative pressure relief valve situated underneath the vaporizer block should the patient's minute volume exceed the fresh gas flow. The subatmospheric pressure required to operate this valve is not stated.

## Results

Seven anaesthetic machines and 14 wall-mounted concentrators installed by May 1987 were in use in seven district hospitals. Eight machines and 16 concentrators were in use in the two referral hospitals. Nitrous oxide was used with the new apparatus only in the larger central hospital.

Anaesthesia was administered with the new apparatus as shown in Tables 1 and 2 during one year from May 1987.

Table 1 shows that in the district hospitals, only 43.5% of all procedures made use of this new apparatus, compared with 94% in the one central hospital studied. The reason for this lies in the poor level of training in general anaesthetic techniques in the districts.

**Table 1.** Methods of anaesthesia.

| | Central hospital | District hospital |
|---|---|---|
| Malawi model | 8640 | 1655 |
| Existing machine | 35 | ? |
| Ketamine | 240 | 470 |
| Spinal | 41 | 261 |
| Local anaesthetic | 241 | 1120 |
| Other methods | — | About 300 |
| Staff: full-time clinical officers | 6 | None |

The 99 major paediatric cases in Table 2 comprised mainly laparotomies for tumour, bowel obstruction and peritonitis but also included surgery to the spine, chest and heart and cranial surgery. These cases all benefited from the use of a T-piece paediatric system which necessitated the modifications described below.

General anaesthetics were administered on 258 occasions in district hospitals to children under 5 years of age. Approximately 35 used the supplied neonatal resuscitator (paedivalve and Ambu bag) and over 180 cases were performed using ketamine.

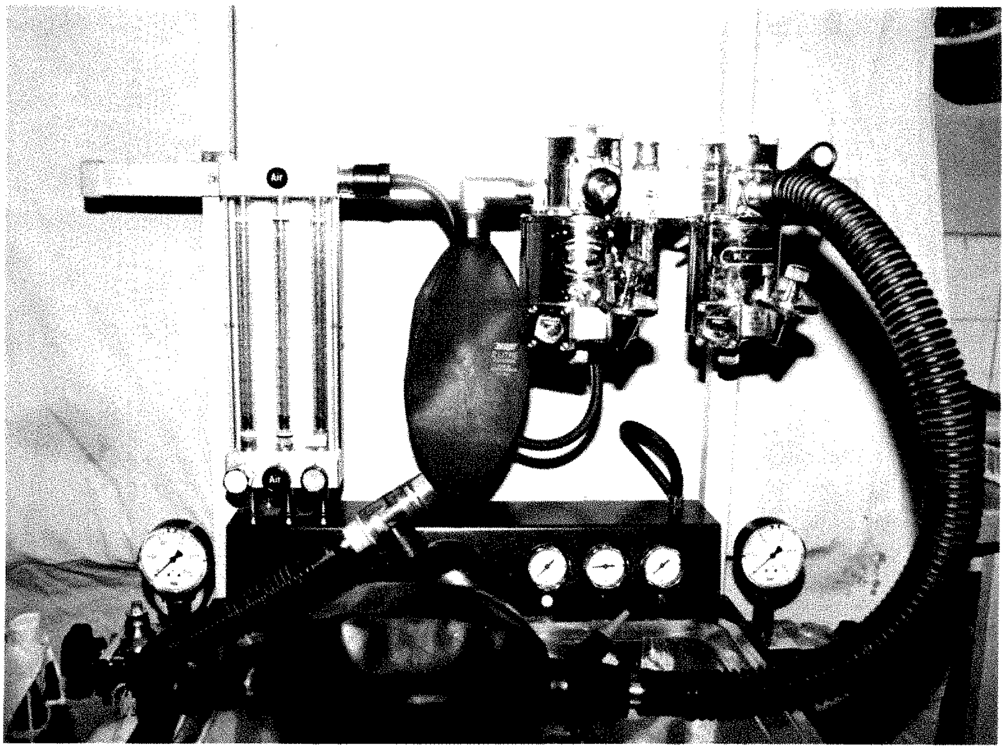


**Fig. 4.** The vaporizer block and patient system.

**Table 2.** Classification of operations.

| | Central hospital | District hospital |
|---|---|---|
| Laparotomy | 295 | |
| Major head, neck, spine | 219 | 88 |
| Thorax | 8 | All major operations 575* |
| Major paediatric | 99 | |
| Minor paediatric | Included in 'others' | 258 |
| Hysterectomy | 93 | 8 |
| Caesarean section | 1261 | 462 |
| Minor gynaecological | 3042 | Included in 'others' |
| Eye | 490 | 60 |
| All others | 3690 | 2399 |
| Totals | 9197 | 3850 |

* Excluding laparotomies and Caesarean section but including hernia, hydrocoele, etc. classified as 'major' in district hospitals.

Thirty-seven percent of 615 adult major cases were deemed by the anaesthetist to require ventilation by a mechanical ventilator which needed the modifications described. All except 16 Caesarean sections were anaesthetised with the apparatus in the manufacturer's intended mode, using spontaneous ventilation with ether through the Ambu bag. The 16 exceptions were severe pre-eclamptics who received mechanical ventilation, as above. Additionally, three patients were ventilated for respiratory failure postoperatively (two) or for Guillain-Barré syndrome (one). Approximately 40% oxygen was given from the concentrator which was used to power a Manley ventilator.

One physician anaesthetist (the author) and six fulltime clinical officer anaesthetists gave anaesthetics in the central hospital. Anaesthesia was given by a variety of clinical officers and medical assistants in the districts, some with 6 months' training but most had no formal training in anaesthesia.

The concentrator requires electricity to function and interruptions to the supply are a frequent event in most rural areas. However, in practice it was found that lack of electric light and autoclaving facilities are more limiting for surgery than failure of the oxygen supply. In the districts, where ether was the only volatile agent in use, air is acceptable for most cases. Emergency oxygen cylinders were not available, though pin-index yokes were fitted to the machines for oxygen and nitrous oxide.

Theatre oxygen consumption from existing 'bull-nose' cylinders was cut virtually to zero and overall oxygen consumption (including wards) for district hospitals was reduced to between a quarter and a half of previous levels. Overall, oxygen consumption for central hospitals was reduced by about a half. The reasons for the continued use of cylinder oxygen included: insufficient concentrators for patients who required oxygen on the wards and reluctance on the part of untrained hospital staff to lift the heavy concentrator down from its high bracket (so placed for electrical safety).

### *Problems*

Water condensation was considerable in the air-buffer tanks and the presence of water in the air Rotameter sometimes made it inoperable during wet weather, despite regular twice-daily drainage from the base of the tanks. Water did not cause such a problem in the oxygen pipeline and Rotameter because it is absorbed by the xeolite granules in the concentrator.

The Ohmeda 'Tec' drawover ether vaporizer has a smaller capacity and poorer thermocompensation compared to an EMO so that when high flows are used during induction of anaesthesia the indicated 15% ether decreases to 10–11%, and induction of robust patients requires repeated doses of suxamethonium to be given before an adequate level of etherisation is achieved.

All the Ohmeda 'Tec' drawover halothane vaporizers

**Table 3.** Expected oxygen concentrations.*

| Flow from '$O_2$' Rotameter (litres/minute) | Oxygen (%) |
|---|---|
| 2 | 95 |
| 4 | 91–92 |
| 5 | 74–75 |
| 6 | 65 |
| 8 | 50 |
| 10 | 47 |
| 15 | 28 |

95% oxygen at a flow of 2 litres/minute achieved after 'warm up' of 7–10 minutes from switching on or from flow of 15 litres/minute.

* From S & W technical data.

suffered from severe corrosion of the milled '% Hal' selection wheel and some were completely jammed within a few months in humid locations.

The use of an Ambu bag in place of the Oxford inflating bellows (OIB) produced mixed opinions. Most users preferred the OIB which has a more restful hand position that is important when prolonged hand ventilation may be required. The OIB can deliver a greater minute volume than the Ambu bag, and the air flow resistance is greater through the Ambu bag during spontaneous ventilation (the author measured subatmospheric pressures of 0.2–0.3 kPa during quiet breathing through the Ambu bag compared with no recordable pressure drop across the OIB).

Air flow resistance was made even greater when the concentrator was not working (as might happen during electricity failure) and inspired air had then to be drawn through the negative pressure relief valve. However, these were minor problems; the apparatus was well liked generally and considered an attractive new piece of equipment, robust in construction, and suitable for district hospital use though, as mentioned below, it was elaborate.

For central hospitals, however, the inability to change from drawover to continuous flow to meet the needs of different clinical situations proved a major flaw: satisfactory anaesthesia for the surgical workload shown in Table 2 requires more than drawover techniques and an Ambu bag.

The use of nitrous oxide with the oxygen-enriched air from the oxygen concentrator soon gave rise to several problems. Unless the oxygen flow was limited strictly to 2 litres/minute (including oxygen direct from the nipple outlet) there is a likelihood of hypoxia when nitrous oxide is used, since the oxygen concentration falls off rapidly when the flow from the concentrator exceeds 2–3 litres (Table 3).

Medical assistants and clinical officers familiar with cylinder oxygen supplies were confused by the effects of flow and oxygen concentration. High oxygen concentrations are unnecessary with ether anaesthesia and it was found to be the only safe anaesthetic technique for Caesarean section using this apparatus.

About 15 litres/minute flow is provided when the oxygen flush button is operated and for the first few seconds the oxygen content is high, while the small reserve in the xeolite canisters and internal oxygen reservoir is drained. Thereafter, however, oxygen concentration can decrease to values as low as 28%. There is no indication to the user of the oxygen concentration that is being administered to the patient.

A problem encountered with the paedivalve and Ambu bag was that, because the PPRV had an opening pressure of 0.8 kPa there was appreciable forward flow through the system and this resulted in obstruction to expiration, with vibration of the rubber valve against the exit port whenever the infant minute ventilation decreased below the fresh gas flow. The respiratory efforts of neonates and small or weak infants were also insufficient to operate the valve mechanisms during spontaneous breathing with halothane, and continuous manual ventilation was necessary. The paedivalve and infant resuscitation bag may be better suited to ether, which stimulates ventilation, rather than halothane, and to a true drawover system without any forward gas flow.

### *Reliability*

No major problems were encountered with any of the 30 concentrators installed in either central or district hospitals. One machine blew an internal fuse due to voltage surge. Oxygen delivery checked 8 months after operation by the manufacturers was satisfactory (in accord with the values in Table 3). A further check after one year, showed one machine was not able to produce higher than 80% oxygen and this was ascribed to a dirty internal air filter which required returning the apparatus for service.

Many machines were used all day long, 5 days a week, and also at other times for emergencies. The anaesthetic machine itself also proved well constructed and reliable, though it had few moving parts to go wrong.

## Discussion

It is only necessary in the district hospitals to have the unmodified concentrator (without pipelines, connexions, buffer tanks or Rotameters) and, using the simple oxygen outlet nipple, supply oxygen at up to 5 litres flow/minute to a conventional T-piece reservoir and drawover ether vaporizer mounted on the basic anaesthetic machine. The necessary drillings could be provided and blanked off so that conversion to upgrade the machine could easily be carried out, should the need arise later.

The following modifications were carried out by the author at the principal central hospital on machines under his direct supervision. The modifications enable the apparatus to be used in all the four modes described by Ezi-Ashi[2] by a simple switching of connexions which takes a few seconds.

The vaporizer block has to be mounted on the back bar, and thus the oxygen flush facility is lost. This is a safety feature (see above).

*Modification for use with a Blease-Manley ventilator.* The ventilator supply hose (22 mm female) is connected directly to the Rotameter block so that air, oxygen or nitrous oxide operates the ventilator. The inspiratory outlet of the Manley ('to patient') passes to the selected vaporizer, and thence to the patient (a double-length Manley patient system is needed). The expiratory limb is connected in the usual way. This constitutes a low pressure (patient airway pressure) 'pushover' technique through a drawover vaporizer and consequently vapour concentrations would be expected to be higher than indicated. In practice, with halothane a setting of '0.5%' gives satisfactory results and greater than '1%' is not allowed when using the ventilator mode for fear of overdose. Measurements of the vapour concentrations under these conditions were not made because the necessary apparatus was not available. The PPRV is immobilised.

*Modification for use with a T-piece paediatric system.* The vaporizer block is connected directly to the Rotameter block by a special female–female connector consisting of two catheter mounts joined back to back. Continuous flow now passes through the selected vaporizer and the paediatric system is connected in the usual way.

The vaporizer block supply hose, now hanging loose, is simply capped onto the vaporizer not in use, which closes the two remaining routes for gas to escape in one manoeuvre.

The PPRV is also immobilised on this modification. Positive pressure relief, which is essential when the drawover mode is used to avoid continuous flow leading to a jammed valve (and consequent risk of pulmonary barotrauma) is achieved reliably, and at lower pressure than 0.8 kPa. It is accomplished by cutting a hole in the bottom of the reservoir bag, to make it into an open-ended reservoir limb.

*Extra vaporizer.* A drawover vaporizer for trichloroethylene was fitted in series with the halothane vaporizer. The 'Goldman' vaporizer, used since it was readily available in sufficient numbers, worked well when filled with trichloroethylene. This modification enabled the machine to be used as a Triservice apparatus.

*To ensure against hypoxic gas mixtures.* Rotameters should be labelled 'oxygen-enriched air' and an oxygen analyser built into the equipment.

## Conclusions

The availability of oxygen, especially to outlying hospitals, was greatly improved by the concentrators, and the cost of oxygen to the health budget was reduced to between a half and quarter of the cost of cylinder oxygen.

The use of a domestic oxygen concentrator with a combined continuous flow and drawover anaesthetic machine is an innovation of great promise for Third World anaesthesia and there will undoubtedly be further developments. The Simonsen and Weel apparatus for Malawi was given much greater versatility by the use of modifications outlined above and they are essential if service in a central hospital is envisaged and the full potential of the concept is to be realised.

The use of nitrous oxide in combination with the oxygen from an oxygen concentrator is potentially hazardous. Serious and prolonged hypoxia is likely to occur (and did occur) in the very setting for which this apparatus is designed: hospitals in developing countries where poorly trained personnel are giving anaesthesia and where previous experience has been with Boyle's machines. Nevertheless after familiarisation with the apparatus the quality of the anaesthetic service in Southern Malawi, particularly at the central hospital, has been considerably improved since the introduction of the Malawi model anaesthetic machine and reliability of the concentrators is so far remarkable.

## Acknowledgments

The author acknowledges the generosity of the Danish International Aid Agency (DANIDA) through which this apparatus was given to Malawi.

I thank Dr I. Wilson, UTH., Lusaka, Zambia for his advice and encouragement in the preparation of this paper and my wife, Joan Fenton, for typing the manuscript.

## References

1. ISO 5356/I Conical connectors for Breathing Systems. International Standards Organisation, Geneva.
2. Ezi-Ashi TI, Papworth DP and Nunn JF. Inhalational anaesthesia in developing countries Part I. The problems and a proposed solution. *Anaesthesia* 1983; **38:** 729–35.
3. *National Atlas of Malawi.* Population density. Malawi Government National Statistical Office 1977: 66.
4. Ezi-Ashi TI, Papworth DP, Nunn JF. Inhalational anaesthesia in developing countries Part II. Review of existing apparatus. *Anaesthesia* 1983; **38:** 736–41.

*Anaesthesia*, 1989, Volume 44, pages 504–508

# Forum

## Serious morbidity attributable to anaesthesia
### Considerations for prevention

T. Pedersen, MD, Senior Registrar, S. H. Johansen, MD, Professor, Department of Anaesthesia, Herlev Hospital, University of Copenhagen, DK-2730 Herlev, Denmark.

**Summary**

*The types and frequency of complications attributable solely to anaesthesia, and which caused serious morbidity and substantial negative outcome, were examined in a prospective study of 7306 anaesthetics. The analysis demonstrated that severe complications and mortality attributable to anaesthesia occurred in 0.59% (1:170) and 0.04% (1:2500) of patients respectively. The data suggest that 'high-risk' patients are more likely to be affected by errors and a substantial negative outcome than more healthy patients. We judged one-third of the anaesthesia-related morbidity to be preventable. Anaesthetists are faced with an increasing number of patients who are at high risk, and who undergo increasingly extensive surgical interventions. Concomitant with the increasing complexity of care and increasing demands on the anaesthetists may be an expected increase in the incidence of errors. Recognition of the importance of human factors in morbidity and mortality attributable to anaesthesia is a necessary first step.*

**Key words**

*Anaesthesia*; audit.
*Complications*; death.

A number of studies of mortality attributable to anaesthesia have been published, but there have been few studies of serious morbidity. This may be due in part to difficulty in defining diseases and physiological events under the heading of 'anaesthesia-attributable morbidity'.

The purposes of this one-year prospective study were to examine the types and the frequency of complications attributable to anaesthesia and to identify possible methods of prevention. Complications considered were those which caused serious morbidity (intermediate or major)[1] and negative substantial outcome.

### *Methods*

Approval from the Human Subjects' Committee of the hospital was obtained to study 7306 consecutive anaesthetics at Herlev Hospital in the period from 1 August 1986 to 31 July 1987.

A special record sheet was designed for the study to gather descriptive information about the patient before admission (pre-operative variables, Table 1), information about events during anaesthesia and surgery and information about the period to the time of discharge from the hospital or to the time of death in hospital.

Important complications attributable to anaesthesia (CAA) are defined as events that occurred in the perioperative period and which caused serious distress, prolongation of hospital stay or both (intermediate morbidity), or permanent disability or disfigurement (major morbidity).[1]

The clinical records, together with an account of the conduct of the anaesthesia, were obtained from the anaesthetists concerned when a complication was identified. This information was examined to determine whether the complication was attributable to anaesthesia or to some other factor. If it was attributable to anaesthesia, then the events were analysed further to determine the precise cause and whether the complication was preventable. Subsequently, three anaesthetists evaluated the causes of the CAA incidents in an attempt to reveal the patterns of possible preventable errors (PE). A subset of incidents consisted of substantial negative outcome (SNO); acute myocardial infarction (AMI); irreversible cerebral damage or death.

Pre-operative evaluation, choice of premedication, monitoring modalities, selection of intra-operative anaesthetic and nonanaesthetic agents and immediate postoperative care were undertaken by a staff anaesthetist who was not one of the authors. Intra-operative management was determined by the pre-operative status and was conducted according to the usual dictates of good anaesthesia care with provisions for amnesia, haemodynamic stability, and optimal pulmonary function.

All data in the study were collected by observers who did not participate in any aspect of patient care. The data were coded, checked for missing or inconsistent values and entered in a computer program by The Copenhagen County Data Processing Department. The statistical analysis was carried out using Chi-squared tests (2 × 2 tables).

---

Accepted 18 November 1988.

0003–2409/89/060504 + 11 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** The most important complications attributable to anaesthesia (those that caused serious distress and required treatment) in 7306 anaesthetics.

| Patient no. | Sex | Age (years) | Anaesthesia | Type | ASA | Surgery | Comments | Outcome |
|---|---|---|---|---|---|---|---|---|
| *Cardiovascular system* | | | | | | | | |
| Cardiovascular insufficiency | | | | | | | | |
| 1 | M | 66 | Epidural | EM | 4 | MA | Cardiac arrest during induction of epidural anaesthesia | Peri-anaesthetic death |
| 2 | M | 74 | Spinal | EM | 3 | MA | Severe hypotension during induction of spinal anaesthesia | AMI |
| 3 | M | 74 | Enflurane | EM | 3 | MA | Severe hypotension and ischaemia during induction with thiopentone | AMI |
| 4 | M | 71 | NL/epidural | EL | 3 | MA | Severe hypotension during anaesthesia | AMI |
| 5 | M | 62 | NL/epidural | EL | 3 | MA | Severe fluctuation in blood pressure during anaesthesia | Cerebrovascular accident and death after 7 days |
| 6 | F | 69 | NL | EL | 3 | MA | Severe hypotension during induction with thiopentone | Interruption of anaesthesia and operation |
| 7 | F | 88 | Thiopentone | EM | 3 | MA | Severe arrhythmia, bradycardia and hypotension during induction | Interruption of anaesthesia and operation |
| 8 | M | 74 | Thiopentone | EL | 3 | MA | Severe hypotension after thiopentone and atracurium | Interruption of anaesthesia and operation |
| 9 | M | 66 | NL | EL | 3 | MA | Asystole after thiopentone, fentanyl and vecuronium | |
| 10 | F | 57 | NL | EL | 2 | MA | Severe overhydration during anaesthesia | Lung oedema during recovery |
| Cardiovascular complications after suxamethonium | | | | | | | | |
| 11 | F | 55 | Halothane | EL | 3 | MA | Asystole after suxamethonium | |
| 12 | F | 53 | NL | EL | 3 | MA | Asystole after suxamethonium | |
| 13 | F | 54 | Enflurane | EL | 3 | MA | Asystole after suxamethonium | |
| 14 | M | 68 | NL | EL | 3 | MI | Severe bradycardia after suxamethonium | |
| 15 | F | 27 | NL | EL | 1 | MA | Severe bradycardia after suxamethonium | |
| 16 | F | 72 | Halothane | EM | 3 | MA | Severe bradycardia after suxamethonium | |
| *Pulmonary system* | | | | | | | | |
| Respiratory insufficiency | | | | | | | | |
| 17 | M | 81 | Enflurane | EM | 3 | MA | Aspiration during induction of anaesthesia | Pneumonia and death after 1 day |
| 18 | M | 72 | NL | EL | 3 | MA | Aspiration during induction of anaesthesia | Pneumonia |
| 19 | F | 24 | NL | EL | 1 | MI | Aspiration during induction of anaesthesia | Pneumonia |
| *Central nervous system* | | | | | | | | |
| Regional anaesthesia and brain dysfunction | | | | | | | | |
| 20 | M | 79 | Spinal | EL | 2 | MI | 25-gauge needle, application was difficult | Severe postspinal headache for 12 days |
| 21 | M | 64 | Spinal | EL | 2 | MA | 25-gauge needle | Severe postspinal headache for several days |
| 22 | M | 67 | Spinal | EL | 2 | MI | 25-gauge needle | Severe postspinal headache for several days |
| 23 | F | 40 | Spinal | EL | 1 | MI | 25-gauge needle | Severe headache for 5 days |
| 24 | F | 33 | Spinal | EM | 1 | MI | 26-gauge needle | Severe postspinal headache treated with caffeine/blood patch |
| 25 | M | 58 | Spinal | EL | 2 | MI | 25-gauge needle | Severe postspinal headache treated with blood patch |
| 26 | M | 64 | Epidural/NL | EL | 3 | MA | Dural puncture | Headache treated with blood patch and analgesics |
| 27 | F | 28 | Epidural/NL | EL | 1 | MA | Dural puncture | Headache treated with blood patch and analgesics |
| 28 | F | 23 | Epidural | EL | 1 | MI | Dural puncture | Headache treated with analgesics |

*Table 1 continued on next page*

## *Results*

Of the total of 7306 anaesthetics, 4407 comprised a modified neuroleptanaesthesia technique, 1854 were inhalational and there were 1054 regional techniques (798 spinal blocks, 169 epidural blocks and 78 peripheral nerve blocks). Forty-three patients were classified as having suffered CAA. The characteristics of these patients are summarised in Table 1.

*Thiopentone.* The commonest single clinical situation that caused cardiovascular complications was 'postinduction hypotension'. Uncompensated hypovolaemia accounted for severe hypotension during induction with thiopentone in four cases (3, 6, 7, 8), all of whom were ASA class 3;

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Awareness under anaesthesia | | | | | | | | |
| 29 | F | 55 | NL | EL | 1 | MA | Consciousness at the end of anaesthesia (bronchospasm) | Distress after operation |
| 30 | F | 52 | Enflurane | EL | 2 | MA | Consciousness at the end of anaesthesia (residual curarisation) | Distress after operation |
| 31 | F | 50 | NL | EL | 3 | MA | Consciousness during anaesthesia | Severe anxiety and nightmare after operation that required treatment |
| 32 | M | 35 | NL | EL | 1 | MA | Consciousness during induction of anaesthesia | |
| 33 | F | 26 | NL | EM | 1 | MA | Consciousness during induction of anaesthesia | Distress after operation |
| 34 | F | 24 | NL | EL | 1 | MA | Consciousness during induction of anaesthesia | Severe anxiety after operation that required treatment |
| 35 | F | 41 | NL | EL | 1 | MA | Consciousness during anaesthesia | Distress after operation |
| 36 | F | 54 | NL | EL | 2 | MA | Consciousness during induction of anaesthesia (drug ampoule swap) | |
| Psychic decompensation following anaesthesia | | | | | | | | |
| 37 | F | 26 | Thiopentone | EM | 1 | MI | Uncomplicated course of anaesthesia | Severe postoperative psychic decompensation, deadly fear, and disturbance of perception for several months |
| 38 | F | 41 | Thiopentone | EL | 1 | MI | Uncomplicated course of anaesthesia | Severe psychic decompensation after operation, slept for 2 days, severe anxiety |
| *Miscellaneous* | | | | | | | | |
| 39 | M | 66 | Halothane | EL | 2 | MA | Palsy of nerve after anaesthesia (pressure paresis) | Sequelae for several months |
| 40 | M | 73 | Enflurane | EL | 3 | MA | No tactile sensation in one foot after anaesthesia | Sequelae for a few days |
| 41 | F | 66 | NL | EL | 3 | MA | Necrosis on lips after tracheal intubation | Sequelae and treatment for several months |
| 42 | F | 67 | NL | EM | 2 | MA | Dental injury at intubation | |
| 43 | F | 52 | Halothane | EL | 3 | MA | Dental injury at intubation | |

NL, modified neurolept anaesthesia; EL, elective; EM, emergency; MI, minor surgery; MA, major surgery; AMI, acute myocardial infarction.

one of these developed acute myocardial infarction (AMI).

*Regional anaesthesia.* In one case (1), a patient with septic shock (ASA class 4) died after epidural anaesthesia which caused profound and uncontrollable hypotension. Too large a dose of supplementary epidural analgesia caused severe hypotension in two cases of neurolept anaesthesia (4, 5); one patient developed AMI, and the other was found to have a hemiparesis postoperatively and died subsequently. Spinal anaesthesia caused severe hypotension during induction in one case (2), and the patient developed AMI.

*Muscle relaxants.* Four patients had cardiac arrest which appeared to be precipitated by anaesthetic drugs (other than thiopentone and epidural/spinal). Three (11–13) followed suxamethonium and one (9) followed fentanyl/vecuronium. Three patients (14–16) had severe bradycardia after suxamethonium.

One patient (10), graded as ASA class 2, developed pulmonary oedema because of overhydration during anaesthesia, and required mechanical ventilation in the postoperative period.

*Vomiting, regurgitation, inhalation of gastric contents.* This occurred in three patients, two of whom had intestinal obstruction (17, 18) and were graded ASA class 3; the third occurred during gynaecological surgery in a patient of ASA class 1 (19). All three developed pneumonia after operation, and one died in cardiopulmonary failure.

Spinal anaesthesia caused severe postspinal headache in six cases (20–25), which required analgesics and prolongation of hospital stay. Three patients (26–28) who underwent epidural anaesthesia suffered dural puncture, required treatment with blood patch and (or) analgesics and had a prolongation of hospital stay.

Eight patients reported awareness during anaesthesia. Four patients (32, 33, 34, 36) were conscious during induction of anaesthesia; in three, the probable cause was an inadequate supply of nitrous oxide and in the fourth the wrong drug was administered because of an error in identification of ampoules. Two patients (31, 35) recalled conversation between the surgeon and the anaesthetist during operation; two (29, 30) were conscious near the end of the operation, and complained that they felt severe pain caused by surgery. Seven of these patients received modified neuroleptanaesthesia, and seven were women (aged 24–55 years) who underwent gynaecological surgery.

Two women (37, 38) had severe psychological sequelae after normal anaesthesia and surgery. One slept for several days after a short (15-minute) procedure and subsequently required treatment in the Psychiatric Department for several weeks; the diagnosis was of anxiety neurosis. The other had deadly fear and disturbance in perception for some months after anaesthesia.

One patient (39) had palsy of the right ulnar nerve after major abdominal surgery with symptoms for 6 months; another (40) had paresis of the left foot for a few days after general anaesthesia.

No case of equipment failure was recorded in this study.

The preventable human errors are summarised in Table 2. There was no statistically significant difference between grades of anaesthetist in relation to the incidence of preventable errors.

The physical status of elective and emergency patients

**Table 2.** Preventable complications attributable to anaesthesia (CAA) and the staff anaesthetists (SA) ($n = 9$) and anaesthetists in training (AT) ($n = 25$) involved.

| Incident | Total | SA | AT |
|---|---|---|---|
| Inadequate anaesthesia (awareness) | 7 | 4 | 4 |
| Drug overdose (thiopentone, epidural, spinal) | 5 | 4 | 2 |
| Drug ampoule swap | 1 | 1 | — |
| Fluid management | 1 | — | 1 |
| Faulty position on the operating table (pressure paresis) | 1 | — | 1 |
| Faulty position of tracheal tube (severe necrosis of lip) | 1 | 1 | — |
| Preventable CAA | 16 | 10 | 8 |
| Preventable CAA: anaesthetics | 1:454 | 1:204 | 1:556 |

before the incidents which led to a substantial negative outcome or which were associated with preventable error, is summarised in Table 3. There was a statistically significant difference between elective and emergency patients in the incidence of negative outcome, but the incidences of CAA and PE in elective compared to emergency patients were not significantly different.

There were significantly increased incidences of CAA, SNO, and PE in seriously ill patients (ASA 3–5) compared to the healthy and moderately ill patients. Furthermore, there was a higher incidence of SNO after complications attributable to anaesthesia in seriously ill patients.

## *Discussion*

The analytical strategy of the present study was first to examine the frequency and the types of complications in the peri-anaesthetic period attributable to anaesthesia, and then to identify their causes and possible preventability.

The analyses demonstrated an overall incidence of 0.59% CAA in 7306 anaesthetics given during one year. The most common type of CAA was cardiovascular collapse (37%; 16/43), severe postoperative headache after spinal/epidural anaesthesia (21%; 9/43), and awareness during anaesthesia (19%; 8/43). A substantial negative outcome was seen in 14% (6/43) of these patients, and the mortality attributable to anaesthesia was 1 per 2500 anaesthetics. We assessed that 37% (16/43) of the anaesthesia-related morbidity was preventable.

Important CAA occurred in 43 patients. Cardiovascular collapse was seen after induction with thiopentone (four cases), bupivacaine (epidural/spinal anaesthesia; three cases), and suxamethonium (six cases). These types of complication are probably familiar to most anaesthetists, and are 'expected' events to which anaesthetists are trained to react promptly. However, the occurrence of negative outcome suggests that vigilance is not always sufficient to prevent injury.

Epidural or spinal analgesia was complicated by severely decreased cardiovascular function in four patients with physical status ASA class 3–4, and this resulted in negative outcome in all four. Epidural/spinal analgesia may be used in severely ill patients but in the presence of impaired cardiac performance or hypovolaemia, meticulous attention to pre-operative assessment and preparation of the patient and to supervision in the peri-operative period are essential.

Severe bradycardia or cardiac arrest was seen after suxamethonium in six cases. Finer and Nylen[2] reported that the incidence of cardiac arrest during induction of anaesthesia ranged from 1 in 209 in burned patients to 1 in 2744 in other patients who underwent plastic surgery. Various mechanisms have been postulated, including vagal reflexes and potassium flux.[3,4]

We found that in six cases out of the 16 with cardiovascular collapse, the injuries could have been prevented by increased attention. Confirmation of the danger of inadequate preparation is found in the New South Wales (Australia) study of anaesthesia mortality.[5] Inadequate preparation was noted in 150 of 286 deaths directly or indirectly due to anaesthesia; examples included failure to prepare patients adequately for surgery or to assess the initial degree of fluid imbalance. The definition of terms in the Australian study was somewhat different from ours, but the result appears to be the same.

Severe postspinal headache (0.8%) that required treatment with analgesics and caused prolongation of hospital stay occurred in six of the 798 patients who received spinal anaesthesia (25–26-gauge needle) in the present study. Sechzer and Abel[6] found that mild, moderate or severe headache developed after operation in 5.4% of patients who received spinal anaesthesia, when a 22-gauge needle was used.

Awareness under anaesthesia occurred in eight (0.1%) of the 5926 patients who underwent general anaesthesia in our study.

Awareness and recall during anaesthesia and surgery have been reported to occur in as many as 1.2% of surgical patients.[7] Muscle relaxants, inadequate mixture of nitrous oxide and oxygen, use of mechanical ventilators, and various defects in anaesthetic machines have been implicated in the causation of awareness during anaesthesia.[8–10]

Our data suggest that less healthy patients are more likely to be affected adversely by errors and a negative outcome. The incidence of preventable errors in relation to CAA in seriously ill patients (ASA 3 or greater) was six times greater than in patients of ASA grade 1 or 2. All patients with substantial negative outcome were seriously ill before anaesthesia.

The patterns observed in this study were similar to those in the studies of Cooper *et al.*,[11] who suggested that the

**Table 3.** Complications attributable to anaesthesia (CAA), substantial negative outcome (SNO) and preventable errors (PE) for each ASA physical status, emergency and elective cases in relation to negative outcome and preventability.

| Operation | CAA % | *n* | SNO % | *n* | PE % | *n* | SNO:CAA % | PE:CAA % |
|---|---|---|---|---|---|---|---|---|
| Elective ($n = 4852$) | 0.69 | (33) | 0.04 | (2) | 0.27 | (13) | 6.1 (2/33) | 39.4 (13/33) |
| Emergency ($n = 2454$) | 0.41 | (10) | 0.16 | (4) | 0.12 | (3) | 40.0* (4/10) | 30.0 (3/10) |
| Healthy or moderately ill (ASA 1–2) ($n = 6502$) | 0.34 | (22) | 0.00 | (0) | 0.14 | (9) | 0.0 (0/22) | 40.9 (9/22) |
| Seriously ill (ASA 3 or greater) ($n = 804$) | 2.62** | (21) | 0.75** | (6) | 0.87** | (7) | 28.6** (6/21) | 33.3 (7/21) |
| Total | 0.59 | (43)† | 0.08 | (6) | 0.22 | (16) | 14.0 (16) | 37.2 (16) |

* $p < 0.05$ compared with elective patients; ** $p < 0.05$ compared with ASA 1–2 patients; †three patients died.

smaller margin for error in sick patients converts more incidents into a substantial negative outcome. They observed also that 13 of 14 incidents of negative outcome involved one or more type of drug overdose and were associated with inexperience or inadequate training. Surprisingly, we found that only six incidents of preventable error involved anaesthetists in training alone ($n = 25$); the remaining 10 incidents involved staff anaesthetists ($n = 9$).

There are difficulties in epidemiological research into mortality attributable to anaesthesia. Comparison between studies may be invalidated by variations in sampling procedure, the definition of time of death, the peri-operative time period studied, and the patient and hospital populations encompassed.

We found that the mortality attributable to anaesthesia in Herlev Hospital was 1:2500. Studies by Harrison,[12] Utting *et al.*,[13] Lunn and Mushin,[14] Tiret *et al.*,[15] Holland,[16] Cohen *et al.*,[17] and the CEPOD study[18] estimate the mortality attributable to anaesthesia to range from 1:2000 to 1:185 000 operations. Surgical and anaesthetic factors that contributed to death in the CEPOD study were identified by both surgical and anaesthetic assessors, and the incidence of death attributable solely to anaesthesia was rather lower than in studies in which surgical factors were ignored.

The three incidents of death attributable to anaesthesia in our study were in severely ill patients (ASA class 3 or greater), and two were judged to be preventable. Approximately 75% of deaths involve moderately ill to very ill patients,[15,16] and estimates of the contribution of errors to anaesthesia-related mortality vary widely. However, there does appear to be consensus that at least half of the deaths are preventable, given existing medical knowledge and accepted anaesthetic practice. The report by Lunn and Mushin[14] suggested that at least 55% are 'avoidable'.

## *Conclusion*

The incidences of severe complications and death attributable to anaesthesia in our institution are 0.59% (1:170.) and 0.04% (1:2500) respectively. Our data suggest that high risk patients are more likely to be affected by errors and a substantial negative outcome than are more healthy patients. We judged that one third of the anaesthesia-related morbidity was preventable.

Anaesthetists are faced with a high-risk patient population which is subjected to increasingly severe surgical interventions. Concomitant with the increasing complexity of care and increasing demands on anaesthetists and surgeons may be an expected increase in the incidence of errors. Therefore, we need strong indications to develop and use appropriate protocols for pre-operative assessment of patients, and also, as suggested by Cooper *et al.*,[19] more careful pre-operative inspection of equipment and apparatus.

Realisation of the importance of the human factor in morbidity and mortality attributable to anaesthesia is a necessary first step.

## *Acknowledgments*

We are indebted to nurses R. Jensen. A. Refsgaard, and V. Juhl for assistance in the postoperative visits to patients. The study was supported by grants from the Danish Medical Research Council, The Danish Heart Foundation, Lily Benthine Lund Foundation, Director I. Henriksen Foundation, and the Danish Society of Anaesthesiology Foundation.

## *References*

1. Lunn JN. Preventable anaesthetic mortality and morbidity. Report of an international symposium. *Anaesthesia* 1985; **40:** 79.
2. Finer BL, Nylen BO. Cardiac arrest in the treatment of burns, and report on hypnosis as a substitute for anesthesia. *Plastic and Reconstructive Surgery* 1961; **27:** 49–53.
3. Bush GH. The use of muscle relaxants in burnt children. *Anaesthesia* 1964; **19:** 231–8.
4. Belin RP, Karleen CI. Cardiac arrest in the burned patient following succinyldicholine administration. *Anesthesiology* 1966; **27:** 516–22.
5. Craig J, Wilson ME. A survey of anaesthetic misadventures. *Anaesthesia* 1981; **36:** 933–6.
6. Sechzer PH, Abel L. Post-spinal anesthesia headache treated with caffeine. Evaluation with demand method. Part I. *Current Therapeutic Research* 1978; **24:** 307–12.
7. Hutchinson R. Awareness during surgery. A study of its incidence. *British Journal of Anaesthesia* 1961; **33:** 463–9.
8. Waters DJ. Factors causing awareness during surgery. *British Journal of Anaesthesia* 1968; **40:** 259–64.
9. Baraka A, Muallem M. Awareness during anaesthesia due to a ventilator malfunction. *Anaesthesia* 1979; **34:** 678–9.
10. Puri GD, George MA, Singh M, Batra YK. Awareness under anaesthesia due to a defective gas-loaded regulator. *Anaesthesia* 1987; **42:** 539–40.
11. Cooper JB, Newbower RS, Kitz RJ. An analysis of major errors and equipment failures in anesthesia management: considerations for prevention and detection. *Anesthesiology* 1984; **60:** 34–42.
12. Harrison GG. Death attributable to anaesthesia. A 10-year survey (1967–1976). *British Journal of Anaesthesia* 1978; **50:** 1041–6.
13. Utting JE, Gray TC, Shelley FC. Human misadventure in anaesthesia. *Canadian Anaesthetists' Society Journal* 1979; **26:** 472–8.
14. Lunn JN, Mushin WW. *Mortality associated with anaesthesia.* London: Nuffield Provincial Hospitals Trust, 1982.
15. Tiret L, Desmonts JM, Hatton F, Vourc'h G. Complications associated with anaesthesia—a prospective study in France. *Canadian Anaesthetists' Society Journal* 1986; **33:** 336–44.
16. Holland R. Anaesthetic mortality in New South Wales. *British Journal of Anaesthesia* 1987; **59:** 834–41.
17. Cohen MM, Duncan PG, Pope WDB, Wolkinstein CA. A survey of 112 000 anaesthetics at one teaching hospital (1975–1983). *Canadian Anaesthetists' Society Journal* 1986; **33:** 22–31.
18. Buck N, Devlin HB, Lunn JN. *Report of the confidential enquiry into peri-operative deaths.* London: Nuffield Provincial Hospitals Trust and the King Edward's Hospital Fund for London, 1987.
19. Cooper JB, Long CD, Newbower RS, Philip JH. Critical incidents associated with intraoperative exchanges of anaesthesia personnel. *Anesthiology* 1982; **56:** 456–61.

*Anaesthesia*, 1989, Volume 44, pages 509–511

# Hypoxaemia during outpatient dental anaesthesia

N. A. Allen, BChD, General Dental Surgeon, D. J. Rowbotham, MRCP, FFARCS, FFARCSI, Lecturer, W. S. Nimmo, BSc, MD, FRCP, FFARCS, Professor, Department of Anaesthesia, The Medical School, Beech Hill Road, Sheffield S10 2RX.

## Summary

*Eighty children, ASA grade 1, who had outpatient general anaesthesia for tooth extraction were studied. An inhalational induction was performed, with patients receiving halothane, nitrous oxide and either 33% or 50% oxygen. Oxygen saturation was measured throughout the procedure using the Ohmeda Biox 3700 pulse oximeter. No significant difference in the incidence of hypoxaemia was found between the two groups. There was no association between the grade of surgeon or anaesthetist and the incidence of hypoxaemia.*

## Key words

*Anaesthesia*; dental, outpatient.
*Measurement technique*; pulse oximetry.

Hypoxia is a major cause of mortality and serious morbidity associated with dental anaesthesia.[1,2] Pulse oximetry allows noninvasive, reliable and accurate continuous measurement of haemoglobin oxygen saturation in patients who have general anaesthesia.[3,4]

The incidence of hypoxaemia during outpatient dental anaesthesia has been assessed recently using the pulse oximeter. Clapham and Mackie found the Ohmeda Biox 3700 pulse oximeter to be a reliable indicator of impending hypoxaemia in the dental chair.[5] Bone and colleagues[6] found a significant reduction in haemoglobin oxygen saturations in 50% of children who had outpatient dental anaesthesia. The technique used in this and other studies was halothane and nitrous oxide 67%, in 33% oxygen. The aim of our study was to compare the incidence, duration and severity of hypoxaemia in children given 33% or 50% oxygen during anaesthesia for minor dental outpatient procedures.

## *Methods*

Eighty patients undergoing outpatient general anaesthesia for minor dental procedures were studied after ethics committee approval and informed parental consent was obtained. All patients were ASA grade 1 and under the age of 14 years.

*Anaesthesia.* All patients were anaesthetised using halothane and nitrous oxide in oxygen with no premedication. The patients were allocated randomly to one of two groups. Group 1 received 33% oxygen, 67% nitrous oxide and Group 2 50% oxygen, 50% nitrous oxide. A Servomex paramagnetic oxygen analyser was used to confirm the oxygen concentration of the inspired gas before measurements of oxygen saturation were recorded. Anaesthesia was administered using a Bain system with a Goldman nasal mask. Fresh gas flow was three times the estimated minute volume. Halothane, as required by the anaesthetist, up to a maximum of 5% was delivered by a Fluotec Mark III vaporizer. Oxygen 100% was administered to all patients for 3 minutes at the end of the procedure. The same anaesthetic machine was used throughout the study, which took about 3 months to complete.

*Observations.* The finger probe of the pulse oximeter was placed on the patient before induction of anaesthesia until after the patient had recovered consciousness. Oxygen saturation and pulse rate were monitored and recorded continuously throughout by the investigator, out of sight of the anaesthetist. The anaesthetist was informed immediately by the investigator if oxygen saturation decreased below 90%. Specific events during the anaesthetic were recorded. These included induction of anaesthesia, placement of mouth pack, tooth extraction, and respiratory obstruction. Total anaesthetic time, time from induction of anaesthesia to surgery, and from cessation of halothane and nitrous oxide to spontaneous eye opening were recorded. Induction time was recorded as the time from start of anaesthesia to start of surgery. Surgery commenced when breathing was regular, pupils central and limbs relaxed.

The overall assessment of anaesthesia was graded by the investigator using the following scale: 1, no movement during surgery; 2, slight movement, little effect on surgery; 3, marked movement, interfering with surgery; 4, surgery extremely difficult due to movement. Hypoxaemia was defined as an oxygen saturation of less than 90%.

Results were analysed using Student's *t*-test, Chi-squared and Mann-Whitney *U* tests as appropriate.

## *Results*

There was no significant difference between the two groups with respect to age, sex and number of teeth extracted (Table 1).

Time taken for induction, recovery, and the total anaesthetic time is shown in Table 2. The mean

---

Accepted 28 October 1988.

**Table 1.** Patient data.

| | Group 1 ($n = 40$) | Group 2 ($n = 40$) |
|---|---|---|
| Sex M/F | 24/16 | 22/18 |
| Mean age years (SD) | 6.2 (3.0) | 7.1 (2.9) |
| Median number of extracted teeth (range) | 4.0 (1-8) | 4.0 (1–15) |

**Table 2.** Mean induction time, recovery time, total anaesthetic time in minutes (SD).

| | Group 1 (33%) ($n = 40$) | Group 2 (50%) ($n = 40$) |
|---|---|---|
| Induction time, minutes, (SD) | 4.8 (1.4) | 5.1 (1.5) |
| Recovery time, minutes, (SD) | 6.11 (2.8) | 6.24 (2.6) |
| Total anaesthetic time minutes (SD) | 14.5 (4.8) | 14.2 (4.3) |

**Table 3.** The grades of the anaesthetist and surgeon. Number of patients with hypoxaemia is shown in parenthesis.

| Grade of surgeon | Group 1 | Group 2 |
|---|---|---|
| Consultants, Senior registrars | 17 (6) | 14 (2) |
| Registrars, Senior house officers | 11 (4) | 12 (2) |
| Students | 12 (3) | 14 (3) |
| **Grade of anaesthetist** | **Group 1** | **Group 2** |
| Consultants, Senior registrars | | |
| Registrars, | 17 (6) | 17 (3) |
| Senior house officers, Dentists | 21 (6) | 21 (4) |
| Students | 2 (1) | 2 (0) |

**Table 4.** Hypoxaemic patient data.

| | Group 1 (33%) | Group 2 (50%) |
|---|---|---|
| Number of patients with hypoxaemia | 13 | 7 |
| Mean age of hypoxaemic patients (SD) | 5.9 (2.7) | 4.9 (2.0) |
| Median number of extracted teeth (range) | 5 (2–7) | 2 (2–10) |
| Time at less than 90% saturation (% of total anaesthetic time) | 1.73% | 1.72% |
| Median lowest oxygen (range) | 82%<br>(29%–88%) | 86%<br>(77%–89%) |

**Table 5.** Procedures associated with maximum decreases in oxygen saturation.

| Factors | Group 1 | Group 2 |
|---|---|---|
| Induction | 2 (15.4%) | 1 (14.25%) |
| Extractions | 3 (23.1%) | 1 (14.25%) |
| Changing operating sides | 2 (15.4%) | 0 (0%) |
| After operation | 6 (46.2%) | 5 (71.0%) |

induction time for those patients who received 33% oxygen was 4.8 minutes, compared with 5.1 minutes for patients receiving 50% oxygen. This was statistically significant ($p < 0.05$). The recovery and total anaesthetic times did not differ statistically between the groups.

The grades of surgeon and anaesthetist are shown in Table 3. There was no significant association between the incidence of hypoxaemia and the grades of the surgeon or anaesthetist (Chi-squared test). All patients were allocated grade 1 for the quality of anaesthesia with the exception of one patient in Group 1.

Twenty patients became hypoxaemic (Table 4). Seven patients had received 50% oxygen and 13 33% oxygen. The lowest saturations in Group 1 ranged from less than 60% to 88%, and in Group 2 from 77% to 89%. Eleven patients became hypoxaemic postoperatively: six patients from Group 1 and five from Group 2. Table 5 shows the incidence of airway complications and the relationship to the lowest oxygen saturation.

## *Discussion*

The aim of our study was to compare the incidence and severity of hypoxaemia during outpatient dental anaesthesia with 33% or 50% oxygen. The results show that 13 patients who received 33% oxygen became hypoxaemic, and that seven patients who received 50% oxygen became hypoxaemic. The lowest oxygen saturations were recorded in patients who received 33% oxygen. However, the findings were not statistically significant.

One patient out of 50 became hypoxaemic in a previous study of a group of 50 patients who received 30% oxygen in nitrous oxide. Both surgeons and anaesthetists were experienced.[7] Studies using three groups of patients who received 20, 25 and 30% oxygen showed that seven out of 23, five out of 21 and five out of 23 patients respectively, became hypoxaemic. Adults and children were studied; anaesthetists and surgeons were both inexperienced.[8]

Bone and others showed that 50% of the patients anaesthetised with 33% oxygen in nitrous oxide became hypoxaemic.[6] A recent study by Sampaio and others, investigating oxygen saturation in children who received halothane or isoflurane as the volatile agent, showed no incidence of saturation below 90% in those patients who received halothane.[9]

Our patients anaesthetised with 33% oxygen showed a similar incidence of hypoxaemia to those in previous studies, but no studies have investigated patients who received 50% oxygen. There was no significant difference between the grade of surgeon and anaesthetist and the number of hypoxaemic episodes in our study. Previous studies have shown an inverse relationship between experience of the surgeon and anaesthetist and the incidence of hypoxaemia.[8] Induction time was prolonged in those patients who received 50% oxygen. This was statistically, but probably not clinically significant.

Hypoxaemia occurred at three stages, during induction, during extractions, and after operation. Over 50% of the hypoxaemic episodes occurred postoperatively despite 100% oxygen. Tomlin,[2] in his review of dental outpatient deaths over a 6-year period, showed that over one third of the deaths occurred during the recovery period. During induction and surgery, in our study, the anaesthetist was aware usually that hypoxaemia had, or was likely, to occur. Postoperatively, they were less aware of the problem.

It is difficult to avoid some degree of respiratory obstruction during outpatient dental anaesthesia even with experienced operators. Events such as pressure on the mandible by the surgeon during extractions, insertion of pack and prop, and changing of sides are all likely to compromise the patients airway. In theory, increasing the inspired oxygen concentration gives a wider safety margin, due to the increased proportion of oxygen stored in the functional residual capacity of the lung. However, in our study we have failed to show a significant decrease in the incidence and severity of hypoxaemia using 50% oxygen.

*Acknowledgments*

We offer thanks to the anaesthetists, surgeons and nursing staff of the Charles Clifford Dental Hospital, Sheffield for their assistance with this study.

*References*

1. Coplans MP, Curson I. Deaths associated with dentistry. *British Dental Journal* 1982; **153:** 357–62.
2. Tomlin PJ. Death in outpatient dental anaesthetic practice. *Anaesthesia* 1974; **29:** 551–70.
3. Taylor MB, Whitwam JG. The current status of pulse oximetry. *Anaesthesia* 1986; **41:** 943–9.
4. Yelderman M, New W. Evaluation of pulse oximetry. *Anesthesiology* 1983; **59:** 349–52.
5. Clapham MCC, Mackie AM. Pulse oximetry. An assessment in anaesthetised dental patients. *Anaesthesia* 1986; **41:** 1036–8.
6. Bone ME, Galler D, Flynn PJ. Arterial oxygen saturation during general anaesthesia for paediatric dental extractions. *Anaesthesia* 1987; **42:** 879–82.
7. Al-Kishali T, Padfield A, Perks ER, Thornton JA. Cardiorespiratory effects of nitrous oxide:oxygen:halothane anaesthesia administered to dental outpatients in the upright position. *Anaesthesia* 1978; **33:** 184–8.
8. Walsh JF. Training for day-case dental anaesthesia. Oxygen saturation during general anaesthesia administered by dental undergraduates. *Anaesthesia* 1984; **39:** 1124–7.
9. Sampaio MM, Crean PM, Keilty SR, Black GW. Changes in oxygen saturation during inhalational anaesthesia in children *British Journal of Anaesthesia* 1988; **61:** 498P.

---

*Anaesthesia*, 1989, Volume 44, pages 511–514

# Occupational exposure to nitrous oxide in four hospitals

W. M. Gray, BSc, PhD, Principal Physicist, West of Scotland Health Boards, University Department of Anaesthesia, Western Infirmary, Glasgow G11 6NT.

## Summary

*Diffusive samplers were used to measure the exposure of the anaesthetist, anaesthetic assistant and circulating nurse to nitrous oxide in every operating theatre of four Glasgow hospitals. Each theatre was surveyed over 1 or 2 weeks; samples were taken during every operating session. The exposures were in general surprisingly high. The anaesthetist's exposure was greater than 100 ppm on more than half the occasions, while in two of the hospitals the anaesthetic nurse's exposure was greater than 100 ppm on about half the occasions. The study underlines the need for theatre ventilation systems and scavenging equipment to be properly maintained and for scavenging facilities to be used effectively. It is concluded that regular monitoring of staff exposures is required to check the effectiveness of antipollution measures.*

## Key words

*Anaesthetics, gases*; trace concentrations.
*Equipment*; exhaust systems.

It is over 10 years since anxiety about the health risk of operating room contamination by anaesthetic gases[1] prompted the Departments of Health in the United Kingdom to advise health authorities on the need for effective scavenging.[2] Many hospitals have complied with this advice, and most operating theatres in Britain are now equipped with scavenging facilities. Several groups have shown that the introduction of scavenging can bring about dramatic reductions in the levels of operating theatre pollution,[3–6] but less attention has been paid to the assessment of the extent to which the potential benefits of scavenging are realised in normal anaesthetic practice. The purpose of this study was to measure the exposures to nitrous oxide of staff working in operating theatres where scavenging facilities were routinely available.

*Methods*

*Hospitals surveyed*

Surveys were carried out between April 1984 and March 1986 in the following hospitals in the Greater Glasgow Health Board Area.

*The Western Infirmary and Gartnavel General Hospital.* These are part of the same administrative unit although on separate sites, and are served by the same anaesthetic team. They constitute together a large teaching centre associated with Glasgow University and have 17 operating theatres. All of the theatres and the associated anaesthetic rooms were equipped with scavenging facilities; in all but four, the equipment was the BOC Mk I (low flow) active system, while in the remainder it was a passive system venting

---

Accepted 30 December 1988.

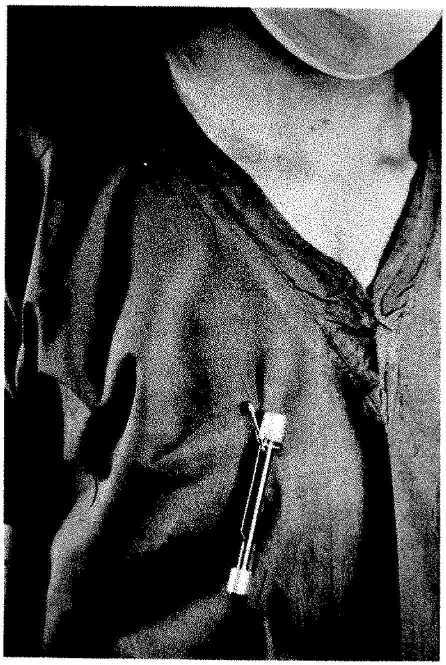


**Fig. 1.** Diffusive sampler as worn for the measurement of occupational exposure to nitrous oxide.

**Table 1.** Summary of exposure measurements in the Western Infirmary and Gartnavel General Hospital (17 theatres).

| | Number of samples | $N_2O$ exposure/ppm | | | Number of samples > 100 ppm |
|---|---|---|---|---|---|
| | | Mean | (SD) | Range | |
| Anaesthetist | 89 | 169 | (217) | 16–1580 | 45 (51%) |
| Operating department assistant | 75 | 59 | (55) | 4–343 | 10 (13%) |
| Circulating nurse | 89 | 40 | (35) | 3–189 | 6 (7%) |
| Background | 89 | 49 | (50) | 4–250 | 10 (11%) |

**Table 2.** Summary of exposure measurements in the Western Infirmary and Gartnavel General Hospital in theatres *with* forced ventilation (14 theatres).

| | Number of samples | $N_2O$ exposure/ppm | | | Number of samples > 100 ppm |
|---|---|---|---|---|---|
| | | Mean | (SD) | Range | |
| Anaesthetist | 69 | 168 | (232) | 17–1580 | 34 (49%) |
| Operating department assistant | 56 | 61 | (46) | 12–213 | 9 (16%) |
| Circulating nurse | 69 | 39 | (35) | 5–189 | 4 (6%) |
| Background | 69 | 42 | (41) | 5–248 | 5 (7%) |

**Table 3.** Summary of exposure measurements in the Western Infirmary and Gartnavel General Hospital in theatres *without* forced ventilation (three theatres).

| | Number of samples | $N_2O$ exposure/ppm | | | Number of samples > 100 ppm |
|---|---|---|---|---|---|
| | | Mean | (SD) | Range | |
| Anaesthetist | 20 | 172 | (159) | 16–696 | 11 (55%) |
| Operating department assistant | 19 | 52 | (76) | 4–343 | 1 (5%) |
| Circulating nurse | 20 | 46 | (36) | 3–131 | 2 (10%) |
| Background | 20 | 73 | (36) | 4–250 | 5 (25%) |

**Table 4.** Summary of exposure measurements in the Royal Hospital for Sick Children (four theatres).

| | Number of samples | $N_2O$ exposure/ppm | | | Number of samples > 100 ppm |
|---|---|---|---|---|---|
| | | Mean | (SD) | Range | |
| Anaesthetist | 19 | 622 | (1158) | 38–5120 | 17 (89%) |
| Anaesthetic nurse | 18 | 155 | (130) | 22–408 | 12 (67%) |
| Circulating nurse | 17 | 56 | (24) | 18–105 | 1 (6%) |
| Background | 19 | 63 | (39) | 8–173 | 2 (11%) |

**Table 5.** Summary of exposure measurements in the Southern General Hospital (five theatres).

| | Number of samples | $N_2O$ exposure/ppm | | | Number of samples > 100 ppm |
|---|---|---|---|---|---|
| | | Mean | (SD) | Range | |
| Anaesthetist | 15 | 310 | (341) | 72–1350 | 12 (80%) |
| Anaesthetic nurse | 15 | 126 | (96) | 23–326 | 7 (47%) |
| Circulating nurse | 15 | 86 | (53) | 17–204 | 5 (33%) |
| Background | 15 | 88 | (59) | 18–254 | 6 (40%) |

**Table 6.** Summary of exposure measurements in the Institute of Neurological Sciences (three theatres).

| | Number of samples | $N_2O$ exposure/ppm | | | Number of samples > 100 ppm |
|---|---|---|---|---|---|
| | | Mean | (SD) | Range | |
| Anaesthetist | 16 | 97 | (36) | 26–187 | 5 (31%) |
| Operating department assistant | 9 | 63 | (26) | 19–100 | 0 (0%) |
| Circulating nurse | 8 | 24 | (9) | 11–37 | 0 (0%) |
| Theatre background | 9 | 37 | (13) | 17–58 | 0 (0%) |
| Anaesthetic room background | 9 | 82 | (34) | 31–149 | 1 (11%) |
| Anaesthetic room/theatre | 9 | 2.27 | (0.77) | 1.6–3.8 | |

through an external wall. All of the theatres with active scavenging, and one with passive scavenging, along with their anaesthetic rooms, were equipped with forced ventilation systems. The remaining three theatres and anaesthetic rooms had no forced ventilation; in one of these theatres, some natural ventilation was provided by grilles connected by a duct to an outside wall, while, in the other two, natural ventilation was sometimes provided by opening doors and windows.

*The Royal Hospital for Sick Children.* This is a regional paediatric hospital with four operating theatres. All theatres and anaesthetic rooms were fitted with the BOC Mk II (high flow) active scavenging system, and were provided with forced ventilation.

*The Southern General Hospital* is a general hospital with five operating theatres. The theatres and anaesthetic rooms were fitted with the BOC Mk I scavenging system, and provided with forced ventilation.

*The Institute of Neurological Sciences* is the Regional centre for neurosurgery and has three operating theatres. The theatres, but not the anaesthetic rooms, were fitted with a scavenging system installed by the hospital engineers and attached to the hospital vacuum system, while both theatres and anaesthetic rooms were provided with forced ventilation.

No attempt was made during the surveys to monitor the anaesthetists' techniques or the extent to which they made use of the available scavenging facilities. Neither was the performance of the theatre ventilation systems measured.

### *Monitoring technique*

Occupational exposure to nitrous oxide was monitored by means of diffusive samplers (Perkin-Elmer), attached to the theatre tunic near the breathing zone (Fig. 1). Details of the methods used for preparation, calibration and analysis of the samplers, together with an assessment of their performance, are published elsewhere.[7] Samplers exposed to test atmospheres in the laboratory yielded results with a coefficient of variation of 4.6% (78 degrees of freedom), while samplers worn by operating theatre staff gave a coefficient of variation of 10.9% (20 degrees of freedom).

Each theatre was surveyed for one or two typical working weeks. Fresh samplers were worn for each operating session and exposures were measured as a time-weighted average over the duration of the session. Three members of staff were monitored: the anaesthetist, the anaesthetic assistant (operating department assistant or anaesthetic nurse) and the circulating nurse.

A peripheral background measurement was made by means of a sampler attached to a convenient point on the theatre wall.

A background measurement was also carried out in the anaesthetic room in the Institute of Neurological Sciences, and the sampler was left in place for the duration of the operating session.

### *Results*

The survey results are summarised in Tables 1 to 6. The exposures are expressed in parts per million by volume (ppm). There is no statutory limit for occupational exposure to nitrous oxide in Britain, but Norway, Sweden and Denmark have adopted 100 ppm as the statutory limit for an 8-hour time-weighted average exposure;[8–10] 100 ppm has therefore been used as a reference exposure in the tables.

The results from the Western Infirmary and Gartnavel General Hospital (Table 1) show two features common to all of the hospitals surveyed. First, there is a wide range of values for each category of staff; for instance, the anaesthetist's exposure ranged from 16 to 1600 ppm. This was not simply a variation between theatres; many theatres displayed a wide range of values from day to day. The second common feature is that the exposures generally decreased in the order: anaesthetist, anaesthetic assistant, background, circulating nurse. The anaesthetist's mean exposure was 169 ppm, with half of the samples greater than 100 ppm; in contrast, the average exposures of the operating department assistant and the circulating nurse were only about a third and a quarter respectively of the average anaesthetist's exposure.

The results in Table 1 can be split into two subgroups, corresponding to theatres with and without forced ventilation, and this is done in Tables 2 and 3. The mean background level was 76% higher in the unventilated theatres; the difference is significant at the 0.05 level for a one-tailed test but not significant for a two-tailed test (Wilcoxon sum of ranks test, $2p = 0.056$). However, there was no substantial difference in the mean exposures of the three categories of staff between the two groups.

The results from the Royal Hospital for Sick Children (Table 4) display two main points of interest. The anaesthetist received a much higher exposure than found at the Western Infirmary, with a mean value almost four times greater and about 90% of samples greater than 100 ppm. The anaesthetic nurse also had a high exposure, with a mean value similar to that of the anaesthetist at the Western Infirmary. The higher levels found in this hospital probably reflect the larger proportion of inhalation inductions and the difficulty of scavenging in paediatric anaesthesia.

The exposures found in the Southern General Hospital (Table 5) were lower than those in the children's hospital but higher than in the Western Infirmary. In particular, the anaesthetic nurse received a mean exposure of more than 100 ppm. The reason for the higher levels here, compared to the Western Infirmary, is not clear.

The Institute of Neurological Sciences gave the lowest exposures of all the hospitals surveyed and was the only hospital in which the mean exposure of the anaesthetist was less than 100 ppm (Table 6). Typical operating sessions in this hospital consist of one or two long cases, and this pattern probably contributed to the relatively low exposures found.

There was a total of 129 occasions on which simultaneous measurements of theatre background and circulating nurse's exposure were made. The correlation coefficient between the two sets was 0.77, but the mean background exposure was 17.7% higher than the mean nurse's exposure; this difference was significant at the 0.005 level (two-tailed paired $t$-test).

### *Discussion*

There is currently some debate about what constitutes a safe level of occupational exposure to nitrous oxide,[11] but there is little doubt that some of the exposures found in the present study are unacceptably high, especially in view of previous reports of dramatic reductions in levels after the installation of scavenging systems.[3–6] Davenport and colleagues[5] found that the installation of scavenging in Northwick Park Hospital reduced the anaesthetist's exposure from a mean value of 411 ppm (range: 120–650 ppm) to a mean value of 24.5 ppm (range: 15–30 ppm). The lowest exposures in the present survey were measured in the Institute of Neurological Sciences, but even here the mean anaesthetist's exposure was four times higher and the maximum value six times higher than the corresponding values found at Northwick Park with scavenging in use. The mean and maximum values in the Western Infirmary were seven and 53 times higher than the Northwick Park values, while in the Royal Hospital for Sick Children the ratios were 25 and 171 respectively.

One factor which may have contributed to the high exposures found in this study is inadequate performance of theatre ventilation systems; this possibility is supported by the similarity of staff exposures for theatres with and without active ventilation in the Western Infirmary and Gartnavel General Hospital (Tables 2 and 3). A second factor may have been inadequate performance of the scavenging systems. A third possibility is that, because scavenging equipment tends to be cumbersome and intrusive, the anaesthetists may not always have used it.

The anaesthetic room is one area where the patient spends only a short time and where the anaesthetist may decide that the use of scavenging is not justified. The background results in Table 6 illustrate the consequences of such a decision. The anaesthetic rooms in the Institute of Neurological Sciences are not fitted with scavenging facilities, but do contain extractor fans. Thus, although the background sampler in the anaesthetic room was left in position for the whole of the operating session, most of the nitrous oxide adsorbed would have been collected during the period when anaesthetic staff were in the room. The high ratio of anaesthetic room background to theatre background (2.3) suggests that, when scavenging is not used in the anaesthetic room, a considerable proportion of the exposure of the anaesthetist and anaesthetic assistant may arise from time spent there, even although this may be relatively short. This effect will be more pronounced in general surgical theatres, where these personnel will usually spend a greater proportion of their time in the anaesthetic room than is the case in this hospital.

There is no reason to believe that Glasgow is exceptional, so it is possible that occupational exposure to waste anaesthetic gases throughout Britain displays a similar pattern to that reported here. This study underlines the need for theatre ventilation and scavenging equipment to be checked and maintained on a regular basis and for steps to be taken to ensure that anaesthetists use scavenging equipment effectively. Further, as in other areas of occupational hygiene,[12] the overall effectiveness of antipollution measures should be checked by regular monitoring of the factor which these measures are intended to control, that is, the exposure of operating theatre staff to waste anaesthetic gases.

## *Acknowledgments*

This work was supported by grants from the Greater Glasgow Health Board. I am also grateful to Mrs J. Stewart for her skilful technical assistance and to the staff who participated in the surveys for their co-operation.

## *References*

1. Vessey MP, Nunn JF. Occupational hazards of anaesthesia. *British Medical Journal* 1980; **281:** 696–8.
2. Department of Health and Social Security. *Health Services Development. Pollution of Operating Departments etc. by Anaesthetic Gases.* Health Circular HC (76) 38, 1976.
3. Oulton JL. Operating room venting of trace concentrations of inhalation anesthetic agents. *Canadian Medical Association Journal* 1977; **116:** 1148–51.
4. McIntyre JWR, Purdham JT, Hosein HR. An assessment of operating room environment air contamination with nitrous oxide and halothane and some scavenging methods. *Canadian Anaesthetists' Society Journal* 1978; **25:** 499–505.
5. Davenport HT, Halsey MJ, Wardley-Smith B, Bateman PE. Occupational exposure to anaesthetics in 20 hospitals. *Anaesthesia* 1980; **35:** 354–9.
6. Krapez JR, Saloojee Y, Hinds CJ, Hackett GH, Cole PV. Blood concentrations of nitrous oxide in theatre personnel. *British Journal of Anaesthesia* 1980; **52:** 1143–8.
7. Gray WM, O'Sullivan J, Houldsworth HB, Musgrave N. The use of diffusive samplers to monitor occupational exposure to waste anaesthetic gases. In: Berlin A, Brown RH, Saunders KJ, eds. *Diffusive sampling. An alternative approach to workplace air monitoring.* London: Royal Society of Chemistry, 1987: 89–92.
8. *Administrativa normer for forurensninger i arbeidsatmosfaere. Veiledning till arbeidsmiljøloven.* Bestillingsnr. 361. Oslo: Direktoratet for Arbeidstilsynet, 1981.
9. *Arbetarskyddsstyrelsens kungörelse om hygieniska gränsvärden.* AFS 1981: 8. Stockholm: Liber Tryck, 1981.
10. *Arbejdstilsynets liste over hygiejniske grænseværdier.* Bilag till publikation nr. 62. Copenhagen: Arbejdstilsynet, 1981.
11. Sharer NM, Nunn JF, Royston JP, Chanarin I. Effects of chronic exposure to nitrous oxide on methionine synthase activity. *British Journal of Anaesthesia* 1983; **55:** 693–701.
12. Leidel NA, Busch KA, Lynch JR. *Occupational Exposure. Sampling Strategy Manual.* DHEW (NIOSH) publication no. 77-173. Cincinatti: National Institute for Occupational Safety and Health, 1977.

*Anaesthesia*, 1989, Volume 44, pages 515–536

# Correspondence

**Anaphylaxis** 516
*M.M. Fisher, MD, FFARCS*
*E.S.K. Assem, PhD, FRCP, FRCPath* 517
**Gastric effects of cytokines** 518
*R.D. Evans, FFARCS*
**The treatment of hyponatraemia** 518
*D. Liu, FFARCS and I. Farquhar, FFARCS*
**Malignant hyperthermia in the Wolf–Hirschhorn syndrome** 519
*F.R. Ellis, PhD, FFARCS and P.J. Halsall, MB, ChB*
*R. Ginsburg, FFARCS and G. Purcell-Jones, MRCP, FFARCS* 519
**Phenytoin-induced resistance to vecuronium** 520
*J.D. Gough, FFARCS, A. Smith, MB BS and C.C. Wise, FFARCS*
**Nifedipine and the pressor response to laryngoscopy** 520
*G.D. Puri, MD*
*T.S. Jayalakshmi, MD and S.C. Kale, MD* 520
**Intranasal cocaine/adrenaline during halothane anaesthesia** 521
*K.B. Shankar, MD, H.S.L. Moseley, FFARCS and Y. Kumar, MD*
**A pitfall in the xanthine oxidase hypothesis** 521
*K. Irita, MD, PhD*
**Cyst of epiglottis** 522
*P. McHugh, FFARCS*
**Dose of bupivacaine** 522
*A. Pottage, MB, ChB, FRCPE*
**Pipeline failure** 523
*D.L. Paul, FFARCS*
**Potential hazard of a cracked Rotameter** 523
*O.A. Williams, BM, DA*
**The oesophageal detector device: successful use in children** 523
*N.S. Morton, FFARCS, J.C. Stuart, MB, ChB, M.F. Thomson, FFARCS and M.Y.K Wee, BSc, FFARCS*
**Profile-cuffed tracheal tubes and the Cardiff Cuff Controller** 524
*B.A. Willis, PhD, FFARCS and I.P. Latto, FFARCS*
**Cuff failure of PVC tracheal tubes** 524
*M. Reinders, CRNA and H.R. Gerber, MD*
**A defect in a tracheal tube** 525
*E. McCoy, MB and S. Barnes*
**Cryoanalgesia after thoracotomy** 525
*P.D. Cussons, MA, D.Phil, FRCS*
**Spinal subdural haematoma after spinal anaesthesia** 526
*J.A.W. Wildsmith, MD, FFARCS*
**Epidural fentanyl at 4°C for analgesia after epidural Caesarean section** 526
*M.J. Fairbrass, FCAnaes, K. Jani, FCAnaes and L. Strunin, MD, FCAnaes, FRCP*
**Inadvertent cause of dural tap** 527
*I.G. Johnston, FFARCSI, RAMC*
**Inadvertent paravertebral block** 527
*J. Gilbert, FFARCS, S. Schuleman, MD and T. Sharp, MD*
**Skin preparation and spinal headache** 528
*J.A.W. Wildsmith, MD, FFARCS*
**Lignocaine 2% with adrenaline for epidural Caesarean section** 528
*D. Brighouse, FFARCS and O. Dyar, MB, ChB, DAO, MRCP*
*A.C. Norton, BSc, FFARCS, A.G. Davis, FFARCS and R.J. Spicer, FFARCSI, MRCGP* 529
**Tachyphylaxis and epidural anaesthesia** 529
*A. Ravalia, FFARCS, D. Browne, MB, ChB and P.N. Robinson, FFARCS*
**The distribution of drugs administered using the Bier's technique** 529
*A.C. Beaumont, FFARCS, J. Gallagher, FFARCS, W. Hamann, MD, PhD and J.R. Wedley, FFARCS*
**Further developments of the laryngeal mask** 530
*A.I.J. Brain, FFARCS*
**Use your Brain—to avoid stress?** 530
*R.M. Griffin, FFARCS, P. Dodd, FFARCSI, G.C. Tosh, MB, BS and C. Buckoke, MB, BS*
**Laryngeal mask and patients with chronic respiratory disease** 531
*R.D. Gunawardene, FFARCS*
**Cord examination after thyroidectomy** 531
*V.J. Sarma, FFARCSI*
**On the insulation of needles** 531
*J. Collier, DRCOG, MRCGP and N.H. Kay, BSc, FFARCS*
**Propofol in acute porphyria** 532
*M.J. McNeill, FFARCS, R.K. Parikh, FFARCS and M.R. Moore, BSc, PhD, DSc*
*B. Hodkinson, BSc, FFARCS* 532
**Fits after alfentanil and propofol** 532
*U. Wittenstein and D.J.R. Lyle, FFARCS*
**Delayed allergic response to propofol** 533
*M. Dold and W.H. Konarzewski, FFARCS*
**The use of ketamine in civilian and military surgery** 533
*M. Lippmann, MD and D. Hsu, FFARCS*
*J. Restall, FFARCS, RAMC, A.M. Tully, FFARCS, RAMC, P.J. Ward, MRCS, LRCP, DA, RAMC and A.G. Kidd, MB, BCh, DA, RAMC* 534
**Perished latex** 534
*D.N. Sutton, FFARCS and V.L. Thomas, FFARCS*
*K. Dobson, MSc, FIQA, C. Chem, FRSC* 534
**$CO_2$ measurement and the Minilink system** 535
*A.C. Beaumont FFARCS and J.G. Diamond, FFARCS*

---

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

**Another use of the pulse oximeter** 535
*L. Murdoch, FFARCS and A. Bray, FFARCS*
**A useful tip** 535
*G. Meakin, FFARCS*
**Failure of rectal diclofenac to augment opioid analgesia** 536
*D.R. Derbyshire, FFARCS*
**Potential hazard with Graseby PCAS** 536
*S.F. Jones, FFARCS and M.K. Reeder, BSc, MRCP, FFARCS*
**Antipollution of the future** 536
*Z. Zych, FFARCS*

## Anaphylaxis

The paper by Assem and Ling (*Anaesthesia* 1988: **43**: 958–61) about the use of radioimmunoassay (RAST) to confirm the diagnosis of anaphylaxis to suxamethonium after death is interesting. It was first established in 1967[1] that true IGE-mediated anaphylaxis can occur on first exposure to the drug. The earlier suggestions,[2] that a lack of previous exposure to suxamethonium means that the reactions are 'due to idiosyncracy rather than alergy', is also now recorded in the UK as incorrect (as was the case in the rest of the world many years ago).

Two aspects of this study concern me greatly. The first is the proposition that RAST testing for antibodies to suxamethonium is a possible method to prevent these reactions. This suggestion is neither logical nor scientific and is fraught with medicolegal hazard for the following reasons.

Three methods can be used to detect the drug responsible for an anaphylactic reaction during anaesthesia. Intradermal and prick testing carry the greatest possibility of success and RAST testing is positive in 90% of patients who have anaphylaxis to suxamethonium confirmed by one or other form of skin testing,[3,4] although the incidence of positive tests to the Pharmacia RAST has not yet been determined to my knowledge. None of these investigations has, however, been evaluated as tests before anaphylaxis, only after. It is likely that such tests would be positive however, and the prick test is the simplest and cheapest and could be performed in an emergency, out of hours, or before office anaesthesia when a RAST may be difficult. Indeed the only advantage of a RAST over an *in vivo* cutaneous test is that it can be performed with blood from a patient who has perished.

Anaesthesia is a common event and anaphylaxis to anaesthesia a relatively rare event, with a maximum reported incidence of 1:1500. Whitby[5] has defined criteria which make a screening test valid for a disease. Anaphylaxis to anaesthetic drugs does not meet these criteria.

There is no at-risk group that can be identified with the exception of patients with a history of previous anaphylaxis to anaesthesia.[6] Cross sensitivity between suxamethonium and other relaxants is common and well documented. Suxamethonium appears the most common cause of anaphylaxis to muscle relaxants but other relaxants which may be used as an alternative in a RAST-positive patient may cause an anaphylactic reaction. In addition, positive RASTs for suxamethonium may be found in patients whose allergy is to other relaxants.[3] Thus the anaesthetist who finds a positive RAST would have to resort to other RASTs, which are less reliable and only routinely performed in three laboratories in the world, or prick test the patient. Why not *just* do the prick test?

My major concern is a medicolegal one which has been expressed before. When patients sue anaesthetists who cause an anaphylactic reaction a common part of the complaint is that no tests were performed prior to anaesthesia to establish safety of the drug. This complaint is easily defended at present. There is neither a validated test nor an identifiable at-risk group. The incidence of disease and the frequency of anaesthesia mean no screening test is likely to be cost effective. Assertions in papers such as that of Assem and Ling place the anaesthetist who has not performed a test in jeopardy in the courtroom, where science and logic may take second place to emotive argument. It is imperative that before such suggestions become dogma a controlled trial validates the hypothesis. It is my personal belief that such a trial is not feasible.

Assuming that 50% of general anaesthetics include a relaxant, and multiplying the number of anaesthetics given in the UK alone by the cost of performing a RAST × 50%, one can produce a frightening figure.

Watkins[7] has recently suggested that alcuronium is more of a hazard than is suxamethonium.

Prevention of anaphylaxis to muscle relaxants would at present be more effectively produced by the use of pancuronium instead of suxamethonium, or by the avoidance of suxamethonium for tracheal intubation before the use of long acting relaxants in elective intubation. The key factor in the prevention of mortality remains adequate treatment, which does not consist of hydrocortisone and atropine as in the case quoted, but the rapid and early use of adrenaline and blood volume replacement with large volumes of colloid solution, which is my second concern with the paper.

The patient is further described as an example of cardiac anaphylaxis in which the heart is a primary target organ. It is well known that intracardiac and extracardiac mediators are released in anaphylaxis and that these mediators affect animal hearts and *in vitro* human cardiac muscle, but primary cardiac dysfunction in humans in systemic anaphylaxis is rare, is usually secondary, and is only reported in two patients with normal hearts before cytotrophic antibody-induced anaphylaxis.[8] There is no evidence given in the paper to support the authors' assertion that this reaction is due to a primary cardiac effect.

*Royal North Shore Hospital*
*St. Leonards, NSW 2065,*
*Australia*
M.M. Fisher

### *References*

1. Jerums G, Whittingham S, Wilson P. Anaphylaxis to suxamethonium: A case report. *British Journal of Anaesthesia* 1967; **39**: 73–6.
2. Assem ESK, Frost PG, Lewis RD. Anaphylactic like reaction to suxamethonium. *Anaesthesia* 1981; **36**: 405–10.
3. Harle DG, Baldo BA, Fisher MM. Detection of IgE antibodies to suxamethonium after anaphylactoid reactions during anaesthesia. *Lancet* 1984; **i**: 930–2.
4. Didier A, Benzarti M, Senft M, Charpin D, Lagier F, Charpin F, Vervloet D. Allergy to suxamethonium: Persisting abnormalities in skin tests, specific IgE antibodies and leukocyte histamine release. *Clinical Allergy* 1987; **17**: 385–92.
5. Whitby LG. Screening for disease. Definitions and criteria .*Lancet* 1974: 819–22.
6. Fisher MM, Outhred A, Bowey CJ. Can clinical anaphylaxis to anaesthetic drugs be predicted from allergic history? *British Journal of Anaesthesia* 1987; **59**: 690–2.

7. Watkins J. Some practical considerations. Discussion about a protocol of a controlled trial: induction of anaesthesia and perioperative risk. *Theoretical Surgery* 1988; **3:** 148–151.
8. Raper RF, Fisher MM. Profound reversible myocardial depression after anaphylaxis. *Lancet* 1988; **i:** 386–7.

## *A reply*

Dr Fisher raises a number of points; although I appreciate his medicolegal view and his concern about costs I would like to concentrate on the following.

He takes the point about reactions which occur on first exposure, whether as a result of allergy or idiosyncrasy, out of context. Furthermore, the term 'anaphylactoid reaction' needs to be kept in perspective. The paper quoted[1] described a patient with such a reaction to suxamethonium on first exposure and the demonstration of massive histamine from leucocytes *in vitro* with that drug and of cross-reaction with most of the other neuromuscular blockers. Tubocurarine did not cause release of histamine and was given in a subsequent anaesthetic without adverse effect. It was reasonable to suggest that the case was 'presumably due to an idiosyncrasy rather than allergy' because of the absence of history of prior exposure, the relative lack of 'specificity' of response, and the background knowledge that neuromuscular blockers (NMB) are thought to be able to induce histamine release from tissue mast cells. This latter occurs at least to some extent, but not in our experience from basophil leucocytes from normal subjects and is independent of classical immune mechanisms; this view is supported by a massive literature including some of the papers quoted by Dr Fisher and the paper he referred to as the first reported case.[2] The paper describing the 'first reported case' could not exclude a possible role (or at a least a contribution) of direct histamine release or idiosyncrasy (it also showed false positive intradermal tests in controls). Now that we have a paper RAST of proven value, cases apparently due to idiosyncrasy are largely eliminated by the test for IgE antibodies to the quarternary ammonium group. We have already shown that the characteristics of histamine release from leucocytes (HRL) of patients with 'anaphylactoid' reactions, by NMB, were identical to classical anaphylactic (IgE-mediated) reactions.[3,4] Some response of lymphocytes (stimulation) further supported an immune mechanism.[4] The Prausnitz–Küstner reaction which was extensively used by the French group confirmed the immune mechanism (IgE mediation),[5] but *in vitro* passive sensitisation (which is safe) did not give a clear result.[4] The value of HRL in anaesthetic reactions, and in the study of the underlying mechanisms and structural requirements for histamine release was also established by us.[3,4,6] Even with the availability of such powerful tools, an element of 'idiosyncrasy', direct histamine release or complement activation via the alternative pathway cannot be excluded.

The choline-RAST is not specific to suxamethonium; it is more or less so for the quaternary ammonium group, which is shared by many NMB, although in different configurations.

The incidence of *positive tests* with Pharmacia RAST has been determined and will be reported in due course. It is true that none of the available investigations have been evaluated as tests before anaphylaxis, only after. It is also true that it is likely that such tests would be positive, and that the prick test is the simplest and cheapest and could be performed in the emergency situation, out of hours, or prior to office anaesthesia when a RAST may be difficult. However, it is neither as reliable (particularly with other NMB when false positives occur frequently in normal subjects; false negatives with low concentration also occur)[7] nor as precise as paper RAST. It therefore would not fulfil the criteria of Whitby.[8] To assert that 'the only advantage of a RAST over an *in vivo* cutaneous test is that it can be performed with blood from a patient who has perished' is an exaggeration.

Pancuronium is safer than suxamethonium, but I am not in a position to say that it can be used 'instead'. The question about treatment was answered before (*Anaesthesia* 1989; **44:** 357).

The evidence about cardiac involvement included cardiac ischaemia and possibly the change from marked sinus tachycardia to severe bradyarrhythmia, and the detection of IgE-sensitised cardiac mast cells (autopsy material). The immunohistochemical detail which was then a paper 'in press' has now been published.[9] Dr Fisher knows how difficult it is to answer this question conclusively in individual cases, judging from the two cases (one of which was during induction of anaesthesia) which he has reported[10] and the correspondence relating to them.[11] Other cases with suggestive evidence of cardiac involvement are reported.[12] Studies in animal models (isolated heart, *in vitro*) and on human cardiac tissues *in vitro* are convincing.

*University College,*
*London WC1E 6BT*
E.S.K. Assem

### *References*

1. Jerums G, Whittingham S, Wilson P. Anaphylaxis to suxamethonium. A case report. *British Journal of Anaesthesia* 1967; **39:** 73–7.
2. Assem ESK, Frost PG, Levis RD. Anaphylactic-like reaction to suxamethonium. *Anaesthesia* 1981; **36:** 405–10.
3. Assem ESK. Examples of the correlation between the structure of certain groups of drugs and adverse effects mediated by immune and non-immune mechanisms (with particular reference to muscle relaxants and steroid anaesthetics). In: Bundgaard H, Juul P, Kofod H, eds. *Drug design and adverse reactions*, Copenhagen: Munksgaard, 1977: 209–26.
4. Assem ESK. Reaction to neuromuscular blocking drugs. In: de Weck AL, Bundgaard H, eds. *Allergic reactions to drugs, handbook of experimental pharmacology*, 63. Heidelberg: Springer, 1983: 299–312.
5. Charpin J, Vervloet D, Nizankovska E. Adverse reactions to relaxants. In: Kent JW, Ganderten MA, eds. *Proceedings of XIth international congress of allergology and clinical immunology*. London: MacMillan, 1983: 67–74.
6. Assem ESK. Characteristics of basophil histamine release by neuromuscular blocking drugs in patients with anaphylactoid reactions. *Agents and Actions* 1984; **14:** 435–40.
7. Farrell AM, Gowland G, McDowell JM, Simpson KH, Watkins J. Anaphylactoid reaction to vecuronium followed by systemic reaction to skin testing. *Anaesthesia* 1988; **43:** 207–9.
8. Whitby LG. Screening for disease. Definitions and criteria. *Lancet* 1974; **ii:** 819–22.
9. Assem ESK, Ghanem NS. Demonstration of IgE-sensitized mast cells in human heart and kidney (with colour plate). *International Archives of Allergy and Applied Immunology* 1988; **87:** 101–4.
10. Raper RF, Fisher MM. Profound reversible myocardial depression after anaphylaxis. *Lancet* 1988; **i:** 386–7.
11. Bain RJI. Myocardial depression after anaphylaxis. *Lancet* 1988; **i:** 834–5.
12. Pusey JM, Charlton SM, Skinner JB, Assem ESK. Anaphylactoid reaction to alcuronium. *Anaesthesia* 1987; **42:** 164–7.

## Gastric effects of cytokines

It has become apparent during investigations on the metabolic effects of the protein cytokines tumour necrosis factor $\alpha$ (TNF $\alpha$-cachectin) and interleukin-1$\beta$ (IL-1$\beta$) that both these paracrine hormones are capable of rapid and profound inhibition of gastric emptying. Both are macrophage products and are released in response to infection, trauma and possibly tumour growth,[1,2] and as such may be (or may have been) present in patients about to undergo anaesthesia.

One hour after a single intravenous dose of 0.6 mg/kg of recombinant human TNF$\alpha$ or 0.1 mg/kg of recombinant human IL-1$\beta$ to Wistar rats, absorption of an oral lipid load was measured by administering $^{14}$C-labelled triolein in gastric lavage; 5 hours later, the gastrointestinal tract was removed and homogenised and the absorption calculated by subtracting its remaining (nonabsorbed) radioactivity from the known administered dose.

Control animals (intravenous saline) absorbed 70.0 (SD 2.85)% of the administered load ($n = 7$) whilst TNF$\alpha$ decreased absorption to 23.5 (SD 2.30)% ($n = 4$) and IL-1$\beta$ to 31.8 (SD 4.0)% ($n = 5$) ($p < 0.001$ for both cytokines by Student's *t*-test). Subsequent analysis showed that most of the label persisted in the stomach. Twenty-four hours after TNF administration, lipid absorption was still significantly decreased (58.9, SD 3.93% $n = 5$, $p < 0.05$).

TNF$\alpha$ and IL-1$\beta$ are rapidly emerging as mediators of endotoxic shock, though their release may be common in diverse stress states. Despite having short plasma half lives (approximately 6 minutes) their metabolic effects are known to persist much longer[3] and this seems to include gastric stasis. These data suggest a possible mechanism for the delayed stomach emptying commonly observed in emergency surgical patients, and cautions against presuming the presence of an empty stomach in a previously 'stressed' patient.

*Radcliffe Infirmary,*
*Oxford OX2 6HE*
R.D. Evans

### *References*

1. Beutler B, Cerami A. Cachectin and tumour necrosis factor as two sides of the same biological coin. *Nature* 1986; **320:** 584–8.
2. Dinarello CA, Mier JW. Interleukins. *Annual Review of Medicine* 1986; **37:** 173–8.
3. Beutler B, Milsark IW, Cerami A. Cachectin/tumor necrosis factor: production, distribution and metabolic fate *in vivo*. *Journal of Immunology* 1985; **135:** 3972–7.

---

## The treatment of hyponatraemia

We read with interest the case report by Batra *et al.* (*Anaesthesia* 1988; **43:** 675–6) about the treatment of hyponatraemia, after systemic absorption of water during vesical ultrasonic lithotripsy. The treatment of hyponatraemia is not without risk and we would like to comment on some of the possible problems that may occur.

The morbidity and mortality of hyponatraemia is not precisely known, but two recent surveys have reported death occurring in up to 50% of patients whose serum sodium concentration were reduced to less than 120 mmol/litre in 24 hours;[1,2] nevertheless rapid correction of severe hyponatraemia, (i.e. less than 120 mmol/litre), was implicated in the causation of serious neurological disturbance and, in some instances, central pontine myelinolysis (CPM).[3,4]

Central pontine or extrapontine myelinolysis is a relatively rare neurological disorder distinguished by behavioural changes, confusion, quadriplegia, pseudobulbar palsy and coma.[5] It was thought to have been a nutritional disorder occurring most commonly in malnourished alcoholics.[6] It has subsequently been described in patients with hyponatraemia of diverse origin. These include postoperative hyponatraemia in otherwise healthy patients and diuretic-induced hyponatraemia.[7–9] The diagnosis has been made by computerised tomography (CT) scanning[5] though magnetic resonance imaging (MRI) may be the method of choice.

The rate at which the serum sodium may safely be increased in hyponatraemia remains controversial. Sterns *et al.* found that an increase of greater than 12 mmol/litre/day increased the risk of patients developing CPM.[10] Some believe that an increase of 2 mmol/litre/hour to a level of around 130 mmol/litre is not excessive in symptomatic patients.[5] Furthermore, the variability in individual response to carefully calculated doses of saline make accurate control of serum sodium difficult and frequent monitoring of the serum sodium essential.[3]

When confronted with a patient with severe hyponatraemia, that is, less than 120 mmol/litre, the clinician must weigh the risks of uncorrected hyponatraemia against those of too rapid a correction. It is our opinion therefore that the correction of hyponatraemia with hypertonic (3%) saline should only be undertaken with extreme caution.

*Queen's Medical Centre,*
*Nottingham NG7 2UH*
D. Liu
I. Farquhar

### *References*

1. Arieff AI, Llach F, Massry SG. Neurological manifestations and morbidity of hyponatremia: correlation with brain water and electrolytes. *Medicine* (Baltimore) 1976; **55:** 121–9.
2. Covey CM, Arieff AI. Disorders of sodium and water metabolism and their effects on the central nervous system. In: Brenner BM, Stein JH, eds. *Contemporary issues in nephrology: sodium and water homeostasis. Vol. 1.* New York: Churchill Livingstone, 1978: 212–41.
3. Laureno R, Karp BI. Pontine and extrapontine myelinolysis following rapid correction of hyponatraemia. *Lancet* 1988; **1:** 1439–41.
4. Dubois GD, Arieff AI. Treatment of hyponatraemia: the case for rapid correction. In: Narins RG, ed. *Controversies in nephrology and hypertension.* New York: Churchill Livingstone, 1984: 393–407.
5. Narins RG. Therapy of hyponatremia: does haste make waste? *New England Journal of Medicine* 1986; **314:** 1573–5.
6. Norenberg MD. Treatment of hyponatraemia; the case for a more conservative approach. In: Narins RD, ed. *Controversies in nephrology and hypertension.* New York: Churchill Livingstone, 1984: 379–91.
7. Tomlinson BE, Pierides AM, Bradley WG. Central pontine myelinolysis. Two cases with associated electrolyte disturbance. *Quarterly Journal of Medicine* 1976; **45:** 373–86.
8. Conger JD, McIntyre JA, Jacoby WJ. Central pontine myelinolysis associated with inappropriate anti-diuretic hormone secretion. *American Journal of Medicine* 1969; **47:** 813–7.
9. Thompson PD, Gledhill RF, Quinn NP, Rossor MN, Stanley P, Coomes EN. Neurological complications as-

sociated with parenteral treatment: central pontine myelinolysis and Wernicke's encephalopathy. *British Medical Journal* 1986; **292:** 684–5.

10. Sterns RH, Riggs JE, Schochet SS. Osmotic demyelination syndrome following correction of hyponatremia. *New England Journal of Medicine* 1986; **314:** 1535–42.

## Malignant hyperthermia in the Wolf–Hirschhorn syndrome

We read with interest and disquiet of the suggested relationship between malignant hyperthermia (MH) and the Wolf–Hirschhorn syndrome (*Anaesthesia* 1988; **43:** 386–8). MH in 'very small children' must be extremely rare since we have not had a proband referred of less than 2 years of age to this Unit. The all-important issue is the strength of the diagnosis of MH. We note that no muscle studies were undertaken and so the diagnosis of MH was not confirmed. We understand that this was not the fault of the authors because the parents refused. The authors rightly point out that very small children are not subjected to muscle biopsy procedures for MH screening purposes; however, it is customary to confirm the diagnosis of MH by showing one or other parent to have the MH genotype.

We would also like to comment on the clinical features. Atropine 0.2 mg in a 5.2 kg child is double the normal dose of 20 μg/kg. The temperature changes were surprising since there was no pyrexia for 50 minutes, during which time she received 4% halothane, and the increase up to 42.2°C occurred in the next 20 minutes, when her lungs were ventilated after tubocurarine for paralysis. We do not associate 'spontaneous ankle clonus' with the type of muscle rigidity commonly found during acute MH.

The blood gas changes are unrelated to the pyrexial response and at the crucial time show no metabolic stimulation. A temperature of 42.2°C at 80 minutes and a pH 7.37 and $P\mathrm{aco}_2$ 3.77 kPa at 85 minutes is inconsistent with the gross type of metabolic stimulation required to increase the body temperature more than 4°C in 10 minutes, which the authors claim.

The authors do not mention any corroborative signs such as muscle spasm, tachycardia, arrythymias, hyperkalaemia, myoglobinuria or raised creatine kinase.

We conclude that this child may have had an MH episode, but there are other more likely causes including recurrent chest infection, and atropine and halothane overdosage.

We believe the authors are responsible for reporting a far-from-proved relationship between two rare diseases. Unfortunately all the bibliographic computers will regurgitate this unproved relationship quite uncritically and generations of anaesthetists will be misled.

*St James's University Hospital,* F.R. Ellis
*Leeds LS9 7F* P.J. Halsall

### *A reply*

Thank you for giving us the opportunity to reply to this letter. The all important issue is, as they rightly state, the strength of the diagnosis of MH. They correctly stress the importance of parental muscle biopsy, and the parents are at the moment reconsidering their decision. However, we neither accept the criticisms of the clinical management of this case, nor their suggestions that the hyperpyrexia could have been due to recurrent chest infection or to atropine or halothane overdose. Nor do we agree that the blood gases are inconsistent with the diagnosis.

The child's axillary temperature was noted to be 35.5°C on the morning of surgery. She had been afebrile for the preceding 48 hours with no evidence of chest infection. Premedication with atropine was given to the child at 0745 hours and the increase in temperature was first noticed at 0955, over 2 hours later. The dose of atropine, 0.2 mg, was in strict accordance with the standard premedication regimen used at The Hospital for Sick Children, and is necessary to avoid excessive stimulation of secretions by cyclopropane. It has been employed uneventfully in thousands of cases.

Fraser[1] described three children, aged 7 to 11 years, premedicated with atropine, 10 μg/kg, having eye surgery, who experienced an increase in temperature under halothane anaesthesia, 90 to 120 minutes after induction. Each patient received supplemental atropine, 0.1–0.2 mg peroperatively, wore extra clothing and was heavily draped. Temperatures increased only to 39 and 40°C. Hyperthermia was easily controlled by body exposure, sponging and ice packs. No patient had abnormal blood gases or any sign of muscle rigidity.

Ellis and Halsall appear to have misunderstood the details of the halothane administration stated in our paper. Four percent halothane was given to the child for no more than 5 minutes; after failure of tracheal intubation and suxamethonium, the child's lungs were manually ventilated by facemask at 10 breaths/minute on 2% halothane in oxygen. Spontaneous ventilation returned rapidly and it was at this point that the halothane concentration was increased to 4%. The halothane concentration was reduced to 0.5% immediately after successful intubation, and the child's lungs were ventilated manually for half an hour until venous access was established. The child was then given a dose of tubocurarine and transferred into the operating theatre.

Ellis and Halsall state that the 'blood gas changes are unrelated to the pyrexial response and at the crucial time show no metabolic stimulation'. This is plainly untrue. They have quoted the pH and $P\mathrm{aco}_2$ of our first blood gas estimation but have omitted to note that the base deficit of this sample was 7.8 mmol/litre. The child's temperature hovered around 39.5°C for more than 3 hours in spite of aggressive cooling, during which time a blood gas estimation of pH 6.89, $P\mathrm{aco}_2$ 11.46 kPa and base deficit 15.9 mmol/litre was typical. Blood culture samples were taken at the time and proved subsequently to be sterile.

We agree that the appearance of spontaneous clonus was surprising. However, it was accompanied by intense extensor rigidity of the lower limbs and flexion of upper limbs despite full curarisation. The muscle rigidity relented only after the second dose of dantrolene. No increase in serum potassium was documented, but serum creatine kinase was grossly elevated: regrettably, the laboratory result has been mislaid. The father's CPK was at the upper limit of normal at 197 μmol/litre. Urine samples were collected, but our laboratory did not perform myoglobin estimation.

The views of those with the experience of Ellis and Halsall must be taken seriously, but we consider that there is little doubt on clinical grounds that the diagnosis of MH was correct, and that we were right to draw the attention of your readership to the possibility of this association.

*King's College Hospital,* R. Ginsburg
*London SE5 9RS*
*The General Hospital,* G. Purcell-Jones
*St. Helier,*
*Jersey*

### *Reference*

1. Fraser JG. Iatrogenic benign hyperthermia in children. *Anesthesiology* 1978; **48:** 375.

## Phenytoin-induced resistance to vecuronium

The case report by Drs Hickey, Sangwan and Bevan (*Anaesthesia* 1988; **43:** 757–9) confirms a clinical observation we have made recently that patients receiving chronic phenytoin therapy have increased requirements for the neuromuscular blocking agents pancuronium and vecuronium. This had become more apparent since we have used vecuronium instead of pancuronium as our preferred relaxant in neurosurgical patients. Our technique involves pretreatment with 1 mg/kg intravenous lignocaine 3 minutes before tracheal intubation, followed by thiopentone 4 to 5 mg/kg, alfentanil 1 to 2 mg, and vecuronium 1.5 mg/kg 90 seconds before intubation. Patient's lungs are then hyperventilated with $N_2O/O_2$ or air/$O_2$ and isoflurane, and given alfentanil by bolus and (or) infusion and incremental vecuronium according to visual assessment of train-of-four response using a Bard peripheral nerve stimulator. Monitoring includes arterial and central venous lines, pulse oximetry, airway pressure, end-tidal $CO_2$ and isoflurane concentration, lower oesophageal activity and lower oesophageal temperature (maintained above 35°C).

Vecuronium is shorter acting than pancuronium with a more rapid recovery index, so it has become more apparent that the duration of action of our intubating dose is reduced in patients receiving phenytoin. Not uncommonly patients are virtually fully recovered in 10 to 15 minutes and then display a reduced time interval between additional doses. We now use this shortened duration to the intubating dose as an indication to change to atracurium relaxation, with which we have not so far had any problems.

May we suggest that this drug-induced resistance to pancuronium and vecuronium, is primarily due to enzyme induction? Satisfactory relaxation is virtually always obtained at first after our induction sequence, although we do use a supramaximal dose of vecuronium for intubation. Our clinical impression is that it is primarily the duration of action that is affected by anticonvulsant therapy. This would explain the normal response to atracurium which is eliminated by Hoffman degradation and, therefore, is not affected by enzyme induction. Furthermore, we have observed similar resistance to vecuronium in a patient who received phenobarbitone anticonvulsant therapy, which is well known to produce enzyme induction.

We readily admit that the above observations should be confirmed by closer scientific investigation, but would concur with Drs Hickey, Sangwan and Bevan that atracurium appears to be a reliable clinical option when predictable relaxation is required for surgery in patients who have received phenytoin before operation.

*University Hospital of Wales,*
*Cardiff CF4 4XW*

J.D. Gough
A. Smith
C.C. Wise

## Nifedipine and the pressor response to laryngoscopy

This is a comment on the article by Kale *et al.* (*Anaesthesia* 1988; **43:** 495–7) in which authors found excellent results with the use of sublingual nifedipine 10 mg given one minute before induction. A review of the literature about peak action of sublingual nifedipine reveals that though the onset of action may be seen within 5 minutes of sublingual administration[1,2] the peak action is generally achieved at 20–45 minutes.[3] This means that nifedipine given one minute before induction or 5 minutes before tracheal intubation will produce much less effect at a time when the stress of intubation is maximum; the peak effect will be evident much later. This may lead to hypotension 10–15 minutes after intubation. The cardiovascular status or blood pressure of the patients at that time should be mentioned to eliminate harmful effects of such pretreatment.

The usual antihypertensive and anti-ischaemic medication of both groups were omitted while the treatment group received nifedipine. Is it routine to omit the morning doses of antihypertensives or anti-ischaemic drugs in the authors' practice or was it done specifically for the present study? Would the results have been different if both the groups received their usual morning medication?

*PGIMER,*
*Chandigarh,*
*India 160012*

G.D. Puri

### *References*

1. Erbel R, Brand G, Meyer J, Effert S. Emergency treatment of hypertensive crisis with sublingual nifedipine. *Postgraduate Medical Journal* 1983; **59** (Suppl 3): 134–6.
2. Lacche A, Basaglia P. Hypertensive emergencies: effects of therapy by nifedipine administered sublingually. *Current Therapeutic Research* 1983; **34:** 879–87.
3. Sorkin EM, Clissold SP, Brogden RN. Nifedipine. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy, in ischaemic heart disease, hypertension and related cardiovascular disorders. *Drugs* 1985; **30:** 182–274.

### *A reply*

The onset of action of sublingual nifedipine is 1–5 minutes and its peak effect is after 20–30 minutes of its administration. The action lasts for 4–5 hours. Rather than subject the patient to the stress of laryngoscopy and intubation, at the peak effect, it was thought that the onset of action of the drug would be more suitable to attenuate the pressor response. Dr Puri's objection is that it may lead to hypotension during the peak action of the drug; however, we did not encounter any hypotension in our patients during this period. A similar observaton has been reported by others[1,2] with the same dose.

The patients did not receive their medication on the day of surgery for this study. We usually continue antihypertensive and anti-ischaemic drugs in these patients as a routine.

*All India Institute of*
*Medical Sciences,*
*New Delhi*
*India 110029*

T.S. Jayalakshmi
S.C. Kale

### *References*

1. Beer N, Gallegos I, Cohen A, Klein N, Sonnenblick E, Frishman W. Efficacy of sublingual nifedipine in the acute treatment of systemic hypertension. *Chest* 1981; **79:** 571–4.
2. Halperin AK, Cubeddu LX, Albuquerque NM. The role of calcium channel blockers in the treatment of hypertension. *American Heart Journal* 1986; **111:** 363–82.

## Intranasal cocaine/adrenaline during halothane anaesthesia

We find the paper (*Anaesthesia* 1988; **43:** 356–8) interesting particularly because there is yet no controlled scientific study to provide experimental data about the use of halothane anaesthesia during topical application of cocaine/adrenaline mixture in clinically useful doses in humans.[1] May we be permitted to comment?

Firstly, Delilkan *et al.*[2] found that the increases in mean pulse rate and in the mean systolic blood pressure were higher in the group who received nasal application of cocaine/adrenaline mixtures than in the group who received cocaine alone, whereas in the present study there was no significant difference between pulse rate and blood pressure in the two groups. The amount of cocaine used in these two studies is similar, so the use of halothane in Bromley's study may have prevented the increase of blood pressure and pulse rate after nasal application of cocaine/adrenaline mixtures.[1]

Secondly, is this technique of spontaneous ventilation with 2% halothane used by the authors justified especially when their study showed cocaine levels which approached toxic levels in two patients? The commonly used combination of topical adrenaline and cocaine is widely considered to be a potentially dangerous mixture.[1–5] Experimental animal studies have shown that cocaine potentiates the arrhythmic effects of halothane and adrenaline combinations.[6] The increased carbon dioxide levels which may be associated with spontaneous ventilation could further increase the risk of arrhythmias. The bradycardia observed by Bromley *et al.* in three patients could be due to the effect of cocaine and 2% halothane. Adrenaline, in the presence of possible hypercarbia could have resulted in ventricular ectopics. Our practice is to use controlled ventilation of the lungs with a Bain system (fresh gas flow 100 ml/kg/minute) in all patients who require intranasal cocaine/adrenaline applications during halothane anaesthesia.[1] The arterial carbon dioxide tensions are predictable with the Bain system even in the absence of end-tidal $CO_2$ monitoring.

We studied electrocardiograms during halothane general anaesthesia in 26 patients who had topical applications of 2 ml either 5% cocaine (100 mg) with 1 in 1000 (2 mg) adrenaline or 10% cocaine (200 mg) with 1 in 10 000 (0.2 mg) adrenaline.[1] A critical analysis of the ECGs revealed no serious arrhythmias except junctional rhythm in two patients and broad and bifid T-waves in five. The ECG changes described occurred at 15 minutes after nasal application of cocaine/adrenaline and persisted for up to 30 minutes, during which time the plasma concentrations are at their peak.[7]

*Queen Elizabeth Hospital,*
*Barbados, West Indies*

K.B. SHANKAR
H.S.L. MOSELEY
Y. KUMAR

*References*

1. SHANKAR KB, MOSELEY HSL, GOPWANI H, CLARKE V, SIVARAJAN S, ISHMAEL R. Halothane and topical cocaine/epinephrine. Is it safe in nasal surgery? *Asian Archives of Anaesthesiology and Resuscitation* 1985; **23:** 281–6.
2. DELILKAN AE, GNANAPRAGASAM A. Topical cocaine/adrenaline combination in intranasal surgery—Is it necessary? *Anaesthesia and Intensive Care* 1978; **6:** 328–32.
3. MAYER E. The toxic effects following the use of local anesthetics. *Journal of the American Medical Association* 1924; **82:** 876–85.
4. PEARMAN K. Cocaine: A review. *Journal of Laryngology and Otology* 1979; **93:** 1191–9.
5. SCHENCK NL. Local anesthesia in otolaryngology. A re-evaluation. *Annals of Otology, Rhinology and Laryngology* 1975; **84:** 65–72.
6. KOEHENTOP DE, LIAO JC, BERGEN VAN FH. Effects of pharmacologic alterations of adrenergic mechanisms by cocane, tropolone, aminophylline, and ketamine on epinephrine-induced arrhythmias during halothane–nitrous oxide anesthesia. *Anesthesiology* 1977; **46:** 83–93.
7. VAN DYKE C, BARASH PG, JATLOW P, BYCK R. Cocaine: plasma concentrations after intranasal application in man. *Science* 1976; **191:** 859–61.

---

## A pitfall in the xanthine oxidase hypothesis

This is a comment on the review by Royston (*Anaesthesia* 1988; **43:** 315). Oxygen-free radicals are now believed to play a central role in ischaemia and reperfusion injury. Oxygen-free radicals can be generated by the leak of electrons from mitochondrial and microsomal electron transport chains, nuclear membranes, the metal ion-dependent oxidation of catecholamines and thiol compounds, the arachidonic acid cascade, phagocytic cells and the action of xanthine oxidase. The proposed mechanism of oxygen-free radical generation *via* xanthine oxidase pathway seems very attractive and is mentioned very frequently in review articles.[1–3]

We should, however, pay attention to the different distribution of this enzyme not only among organs but also among species.[4] Xanthine oxidase is abundant in rat intestine (Table 1) and is almost undetectable in the brains of all species examined. Man does not have the enzyme in the heart, lung and skeletal muscles, nor probably in the brain, which suggests that oxygen-free radicals cannot be generated by xanthine oxidase in human organs other than the liver, intestine and kidney. Some investigators propose that allopurinol manifests its action by suppressing radical formation from xanthine oxidase, but it seems reasonable that allopurinol would have beneficial effects by inhibiting the purine loss from ischaemic tissue and facilitating restoration of cellular ATP.[5] Human xanthine oxidase might be more important in the metabolism of drugs such as deoxyacyclovir,[6] halothane[7] and iron.[4]

**Table 1.** Tissues- and species-specific distribution of xanthine oxidase.

| | Species | | |
|---|---|---|---|
| Organs | Man | Dog | Rat |
| Brain | ? | — | ± |
| Heart | — | — | + + |
| Lung | — | + | + + |
| Liver | + + + | + + | + + + |
| Intestine | + + | + + + | + + + + |
| Kidney | + | + + | + + + |
| Skeletal muscle | — | — | ? |

Relative xanthine oxidase activity is shown from the data in reference 4 and other manuscripts not cited.

The following observations favour the possibility that granulocytes-derived free radicals play an important role in ischaemia/reperfusion injury: granulocytes can produce a huge amount of toxic-free radicals upon stimulation; granulocytes are plugged in ischaemic tissue;[8] and prevention of granulocyte adhesion reduces myocardial reperfusion injury.[9]

Simmonds *et al.* have also argued against the oversimplified application of the xanthine oxidase hypothesis to man in a manuscript with a subtitle 'Man is not a mouse!'[10] It should be mentioned that the results obtained by animal studies cannot be directly applied to humans.

*Kyushu University 60,*
*3-1-1 Maidashi,*
*Higashiku,*
*Fukuoka,*
*Japan*

K. IRITA

*References*

1. WEBSTER NR, NUNN JF. Molecular structure of free radicals and their importance in biological reactions. *British Journal of Anaesthesia* 1988; **60:** 98–108.
2. MCCORD JM. Oxygen-derived radicals: a link between reperfusion injury and inflammation. *Federation Proceedings* 1987; **46:** 2402–6.
3. BULKLEY GB. Free radical-mediated reperfusion injury: A selective review. *British Journal of Cancer* 1987; 66–73.
4. PARKS DA, GRANGER DN. Xanthine oxidase: biochemistry, distribution and physiology. *Acta Physiologica Scandinavica* 1986; **548** (Suppl.): 87–99.
5. LASLEY RD, ELY SW, BERNE RM, MENTZER RM JR. Allopurinol enhanced adenine nucleotide repletion after myocardial ischemia in the isolated rat heart. *Journal of Clinical Investigation* 1988; **81:** 16–20.
6. KRENITSKY TA, HALL WW, DE MIRANDA P, BEAUCHAMP LM, SCHAEFFER HJ, WHITEMAN PD. 6-Deoxyacyclovir: a xanthine oxidase-activated prodrug of acyclovir. *Proceedings of the National Academy of Sciences USA* 1984; **81:** 3209–13.
7. SCHIEBLE TM, COSTA AK, HEFFEL DF, TRUDELL JR. Comparative toxicity of halothane, isoflurane, hypoxia, and phenobarbital induction in monolayer cultures of rat hepatocytes. *Anesthesiology* 1988; **68:** 485–94.
8. ENGLER R. Granulocytes and oxidative injury in myocardial ischemia and reperfusion. *Federation Proceedings* 1987; **46:** 2395–6.
9. SIMPSON PJ, TODD RF III, FANTONE JC, MICKELSON JK, GRIFFIN JD, LUCCHESI BR, ADAMS MD, HOFF P, LEE K, ROGERS CE. Reduction of experimental canine myocardial reperfusion injury by a monoclonal antibody (Anti-Mo 1, Anti-CD 11b) that inhibits leukocyte adhesion. *Journal of Clinical Investigation* 1988; **81:** 624–9.
10. SIMMONDS HA, GODAY A, MORRIS GS. Superoxide radicals, immunodeficiency and xanthine oxidase activity: man is not a mouse! *Clinical Science* 1985; **68:** 561–5.

---

## Cyst of epiglottis

This is a report of a case which occurred in our hospital recently. A 22-year-old man was admitted as an emergency with lacerations of his wrists after falling through a plate glass window. He had obvious tendon damage to his left wrist but it was decided that since he had been drinking heavily the operation would be delayed until the next morning. There were no systemic abnormalities and he had no previous anaesthetics.

He was premedicated with oral temazepam 20 mg and droperidol 5 mg one hour before operation. An ECG was connected and an indwelling cannula inserted; anaesthesia was induced with thiopentone 5 mg/kg and suxamethonium 1.5 mg/kg. No abnormality was seen on opening his mouth but when a laryngoscope was inserted it was impossible to see his laryngeal inlet because it was occluded by a large translucent swelling which arose from the right side of his epiglottis. There was no difficulty in lung inflation via a Bain system. A gum elastic bougie was passed with difficulty around the swelling into the trachea and a 9.0 cuffed orotracheal tube railroaded over it.

The anaesthetic and surgery proceeded uneventfully and at the end of the procedure his trachea was extubated easily and no respiratory difficulties ensued. He was referred to the ENT department for further assessment.

Cysts of the epiglottis have been reported in the literature on a few occasions but their incidence is unkown since they are usually benign and asymptomatic. They have various aetiologies and are loosely described[1] as any cystic lesion arising from, or encroaching upon, the epiglottis. The main complications arising from these cysts are acute respiratory obstruction and aspiration of the cyst contents into the lungs. Mason[2] reported two cases with different management in 1987, one of which was aspirated by the resident ENT surgeon and the other which was intubated over a bougie as here. There was no ENT surgeon available in the present case and it was decided not to abandon anaesthesia and surgery because the airway was easy to maintain. It is stressed that these problems, although infrequent, do arise in patients who are apparently normal and that the anaesthetist has to be continually alert to the possibility of a difficult intubation.

*Bassetlaw District General Hospital*
*Worksop,*
*Notts S80 2BN*

P. MCHUGH

*References*

1. PADFIELD A. Epiglottic cysts, a case report and review. *Anaesthesia* 1972; **27:** 84–8.
2. MASON DG, WARK KJ. Unexpected difficult intubation. Asymptomatic epiglottic cysts as a cause of upper airway obstruction during anaesthesia, *Anaesthesia* 1987; **42:** 407–10.

---

## Dose of bupivacaine

We wish to alert anaesthetists to an error which appears in the dosage section of the Marcain (bupivacaine) data sheet and in dosage charts for Marcain issued by Astra Pharmaceuticals Ltd. This error only involves the recommended dosage for caudal blockade in children, where ml has been substituted for mg which has the effect of increasing the dose. The correct recommended dosage is as follows:

for blockade to lower thoracic determatomes ($T_{10}$) 0.3–0.4 ml/kg (0.75–1.0 mg/kg)

for blockade to midthoracic dermatomes ($T_6$) 0.4–0.6ml/kg (1.0–1.5 mg/kg)

All doses refer to the 0.25% concentration (2.5 mg/ml). If, however, the calculated dose exceeds 20 ml, the concentration should be reduced to 0.2% (2.0 mg/ml)

An erratum slip will be included in the next Data Sheet Compendium, and the Department of Health has been informed of the situation. We sincerely regret any confusion that may have been caused by this inadvertent error.

*Astra Clinical Research Unit,*
*10 York Place,*
*Edinburgh EH1 3EP*
A. POTTAGE

## Pipeline failure

A recent incident in theatre highlighted a problem that could occur in other hospitals as a result of changes in existing working practices without full appreciation of the possible consequences.

The patient was a 54-year-old woman who was to have a right internal carotid aneurysm clipped. She received a standard neurolept anaesthetic and her lungs were ventilated with a Cape-Waine Mk III which was adapted for air entrainment. The aneurysm was clipped without incident but during closure of the dura the patient became markedly hypertensive. The cause was traced to a gradual reduction in nitrous oxide delivery, with a flow rate which decreased from 6 to 3 litres/minute. The nitrous oxide pipeline pressure was nearly zero. The other two theatres in the suite were warned by an ODO while the patient was settled with cylinder nitrous oxide. Fortunately, she made an uneventful recovery.

The reason that an almost empty nitrous oxide bank had passed unnoticed soon became apparent. The alarm system for nitrous oxide (but not oxygen) is situated in the unit's porters' box at some distance from the theatres. This had been a reasonable arrangement when the unit had had its own 24-hour pool of porters but with reorganisation of their services the porters had been transferred to a central location which left the pipeline alarm unattended. There was neither subsidiary alarm in theatre nor were the theatre staff aware that the pipeline was unmonitored. The oxygen system is monitored in the main hospital.

A similar situation could occur in other hospitals so it is prudent for all anaesthetic departments to check the location of their pipeline alarms and to ensure that similar changes in organisation do not expose patients to extra risk.

*Western Infirmary,*
*Glasgow G11 6NT*
D.L. PAUL

## Potential hazard of a cracked Rotameter

A Manley ventilator was observed during an emergency appendicectomy in the early hours of a Monday morning to be cycling slightly more slowly than normal for the selected gas flows of 2 litres/minute of oxygen and 4 litres/minute of nitrous oxide for a minute volume of 6 litres. Careful examination failed to reveal any leaks in the tubing connexions and the cause of the problem remained undetected. No further action was taken.

Two days after the initial incident the anaesthetist was rostered for a routine list in the same theatre. It was again noted during the first case that for the usual 6-litre fresh gas flow the ventilator was cycling marginally more slowly than normal. An Engström Eliza gas analyser indicated an inspired oxygen of 60% rather than the approximately 33% expected from the Rotameter setting. This implied that up to 3 litres/minute nitrous oxide was leaking. A further search revealed a 4-cm undisplaced hairline crack in the rear of the nitrous oxide Rotameter which extended from the top of the tube downwards such that gas was able to leak distal to the bobbin.

Anaesthesia was satisfactory on both occasions and awareness was not reported. Had the crack occurred in the oxygen Rotameter a hypoxic mixture would have been administered. Loss of gas distal to the Rotameter bobbin cannot be detected using the single hose Boyle's machine check. Reduced flow from such a cause might be revealed by observing ventilator cycling for low flows of each gas in turn, though a leak from such a small defect would be dependent on back pressure from the ventilator.

Attention is drawn to how easy it was to dismiss the problem on the first occasion—as did presumably the other anaesthetists who had used the machine in the 48-hour period between the writer's observations.

*Northern General Hospital,*
*Herries Road,*
*Sheffield S5 7AU*
O.A. WILLIAMS

## The oesophageal detector device: successful use in children

The oesophageal detector device has been shown reliably to distinguish oesophageal from tracheal intubation in adults intubated with cuffed tubes (*Anaesthesia* 1988; **43:** 27–9). Subsequent correspondence (*Anesthesia* 1988; **43:** 713) suggested that cuff deflation allows clearer differentiation between the two sites. The use of plain tracheal tubes should therefore improve discrimination between oesophageal and tracheal tube placement. We therefore evaluated the efficacy of the oesophageal detector device in children aged 5 to 10 years intubated with uncuffed tracheal tubes using a single blind protocol similar to Dr Wee's adapted for paediatric practice.

Twenty healthy children, ASA grade 1 or 2, aged between 5 and 10 years who were to have elective ENT surgery, where tracheal intubation was required as part of the anaesthetic technique, were studied. Informed written consent was obtained from each child's parent or guardian and local hospital ethics committee approval was obtained. Two identical tracheal tubes were passed, one into the trachea and one into the oesophagus. The position of the left-hand tube was randomised and an observer was brought in to aspirate the left hand tube with the oesophageal detector device.

The children were well matched for age and weight (Table 1). The position of the left hand tube was diagnosed rapidly and correctly in all cases by a variety of staff grades and there were no postoperative sequelae.

Intubation of the oesophagus may be more difficult to detect in children because of their thinner and more compliant chest walls which may give clinical signs that mimic tracheal tube placement (bilateral chest expansion, audible 'breath' sounds). Capnography is very helpful but

**Table 1.** Patient data and results.

| | Position of left-hand tube | |
|---|---|---|
| | Oesophagus ($n$ = 10) | Trachea ($n$ = 10) |
| Mean (SD) age, months | 82.2<br>(16.3) | 88.5<br>(19.1) |
| Mean (SD) weight, kg | 25.1<br>(5.0) | 26.0<br>(6.4) |
| Mean (SD) time to correct diagnosis of tube position (seconds) | 4.30<br>(0.82) | 5.70<br>(2.45) |
| Grade of observer | | |
| *Anaesthetist* | | |
| Consultant | 3 | 5 |
| Senior registrar | 4 | 0 |
| Registrar | 0 | 1 |
| Senior house officer | 2 | 3 |
| *Staff nurse* | 0 | 1 |
| *ENT registrar* | 0 | 1 |

is expensive and is seldom available in the anaesthetic room or the resuscitation area. We have demonstrated in this study that the oesophageal detector device can be used reliably by a variety of grades of personnel in children as in adults. Other workers have been enthusiastic supporters of the use of the device and have adapted the design for their own use (*Anaesthesia* 1988; **43:** 804 and 906). We found the original adult design (50 ml catheter tip syringe, catheter mount and 15 mm connector) worked well in children. Indeed, the use of a smaller syringe could result in more negative pressure being applied to the airway. If the cross-sectional area of the plunger is reduced the aspiration of a given volume will generate greater subatmospheric pressure which could be hazardous in a small child. We found that the plunger need be withdrawn only a small distance (5 ml) to differentiate clearly between oesophageal and tracheal tube placement. We recommend the routine use of this simple, inexpensive device wherever tracheal intubation is performed in both adults and children. We consider that it has the potential to become one of the routine safety checks to confirm tracheal tube placement.

*Royal Hospital for Sick Children,*
*Glasgow G3 8SJ*

N.S. MORTON
J.C. STUART
M.F. THOMSON
M.Y.K. WEE

### Profile-cuffed tracheal tubes and the Cardiff Cuff Controller

A comparison was made in our previous study[1] between tracheal tube cuff pressure immediately after inflation (ICP) and the minimum cuff pressure (MCP) to maintain a leak-free seal between trachea and cuff. The latter measurements were made using the Cardiff Cuff Controller and the tracheal tubes were Portex standard-cuffed tubes.

Our conclusions were that syringe inflation often produces grossly overinflated cuffs, that cuff-pressure monitoring may be performed simply using the Cuff Controller and that the male and female tracheas may differ in diameter by more than the 9 mm to 8 mm difference in tube sizes.

We have now made similar measurements on Portex profile-cuffed tracheal tubes, size 9 mm for adult males ($n$ = 20) and 8 mm for adult females ($n$ = 28).

There is a tendency as with standard cuffs to overinflate the profile cuffs when syringe inflation is used. The pressure difference (ICP − MCP) is statistically very highly significant for males and females.

The minimum cuff pressure data for profile and standard cuffs in females does not differ significantly (1.0 kPa and 1.2 kPa). The minimum cuff pressure in adult male patients was significantly lower in profile compared with standard cuffs. (1.0 kPa and 5.2 kPa).

**Table 1.** Mean (SEM) kPa.

| | ICP | MCP | ICP − MCP |
|---|---|---|---|
| Females $n$ = 28 | 11.9 (1.3) | 1.0 (0.1) | 10.9* (0.1) |
| Males $n$ = 20 | 10.3 (1.6) | 1.0 (0.1) | 9.3* (1.6) |

* $p < 0.0001$ Paired Wilcoxon signed rank test.

These results mean that in adult males the profile-cuffed tracheal tubes have some advantage over the standard-cuffed tubes since lower pressures are necessary to maintain a leak-free seal between cuff and trachea. However as a result of their shape, the pressure in a profile-cuffed tube is more representative of the pressure exerted on the tracheal wall and prolonged overinflation of such a cuff may be more harmful to the tracheal mucosa than a standard cuff.

*University Hospital of Wales,*
*Cardiff CF4 4XW*

B.A. WILLIS
I.P. LATTO

#### *Reference*

1. WILLIS BA, LATTO IP, DYSON A. Tracheal tube cuff pressure. Clinical use of the Cardiff Cuff Controller. *Anaesthesia*, 1988; **43:** 312–14.

### Cuff failure of PVC tracheal tubes

We read with interest the paper by Walmsley *et al.* (*Anaesthesia* 1988; **43:** 399–401) which reported on cuff failures of polyvinyl chloride (PVC) tracheal tubes in contact with sprayed lignocaine. We have used 4% plain lignocaine solution routinely for tracheal anaesthesia for many years and no overt cuff failure had been detected. Different brands of PVC tracheal tubes are used so we were interested to investigate their susceptibility to damage by different lignocaine preparations.

Twenty 8.5-mm Endosoft tracheal tubes (Asid Bonz-Comp., Boeblingen, W. Germany) and 20 8.5-mm Lo-Pro tracheal tubes (Mallinckrodt Laboratories, Athlone, Ireland) were tested with a similar experimental design as in the report of Walmsley. We tested (Group D) lignocaine gel 2% (Astra Pharmaceuticals). In Group A normal saline was used instead of water. A five-point scoring system was used (1 = no leak, 2 = leak, 3 = clouding, 4 = softening, 5 = blistering) to judge any changes of the visual and (or) physical appearance of the cuffs. The results are summarised in Table 1.

There was one pinhole leak in the cuff of a Mallinckrodt tube in Group C (Astra lignocaine spray). The results indicate that most of the physical damage at the cuffs of PVC tracheal tubes is caused by additives to

**Table 1.**

| Score | Normal saline (A) | | Lignocaine 4% (B) | | Lignocaine spray (C) | | 2% lignocaine gel (D) | |
|---|---|---|---|---|---|---|---|---|
| | Lo-Pro $n = 5$ | Endosoft $n = 5$ | Lo-Pro $n = 5$ | Endosoft $n = 5$ | Lo-Pro $n = 5$ | Endosoft $n = 5$ | Lo-Pro $n = 5$ | Endosoft $n = 5$ |
| 1 | 5 | 5 | 5 | 5 | 4 | 5 | 5 | 5 |
| 2 | | | | | 1 | | | |
| 3 | 3 | | 2 | | 5 | 5 | 4 | 4 |
| 4 | | | | | 1 | 1 | | |
| 5 | | 4 | | 5 | 1 | 5 | | 5 |

Score: 1 = no leak; 2 = leak; 3 = clouding; 4 = softening; 5 = blistering.

the lignocaine preparations and the commercial Astra-lignocaine spray causes the most damage. When PVC tracheal tubes are to be used plain 4% lignocaine solution applied with a long tip-occluded multiple-orifice needle seems to be the method of choice for topical tracheal anaesthesia.

Recent reports of damage to plastic material by isoflurane[1,2] suggest another mechanism for cuff failure. To elucidate this problem liquid isoflurane, enflurane and halothane were therefore applied to the cuff surface and any leaks and (or) changes in the visual appearance noted. There was a slight clouding of the cuff, but no leak on inflation of the cuffs upto 2 kPa pressure was observed. Thus commercial lignocaine spray can so far be identified as the only cause of chemically induced physical disruption of the cuffs.

*EVK Hospital,*
*PO Box 2940,*
*D4000 Dusseldorf,*
*West Germany*

M. Reinders
H.R. Gerber

*References*

1. Maltry DE, Eggers GWN. Isoflurane-induced failure of the Bentley-10 oxygenator. *Anesthesiology* 1987; **66:** 100–1.
2. Cooper S, Levin R. Near catastrophic oxygenator failure. *Anesthesiology* 1987; **66:** 101–2.

## A defect in a tracheal tube

A defect was felt, rather than seen, on the convex surface of a Sheridan CF style tracheal tube after it was cut to 25 cm.

The defect was difficult to see without close inspection and began 15.5 cm from the distal tip. It extended 6.0 cm, tapered at both ends and was 2.5 mm at its widest point. Part of the material of the tube was missing, including the X ray line, so the defect appeared to be a cut rather than a split. There was no damage to the tube package.

The tube and package were returned to the makers, who reported it as a rare and random occurence with no obvious cause.

The defect was felt rather than seen; had it occurred closer to the distal end, it might have gone unnoticed.

*The Ulster Hospital,*
*Belfast BT16 0RH*

E. McCoy
S. Barnes

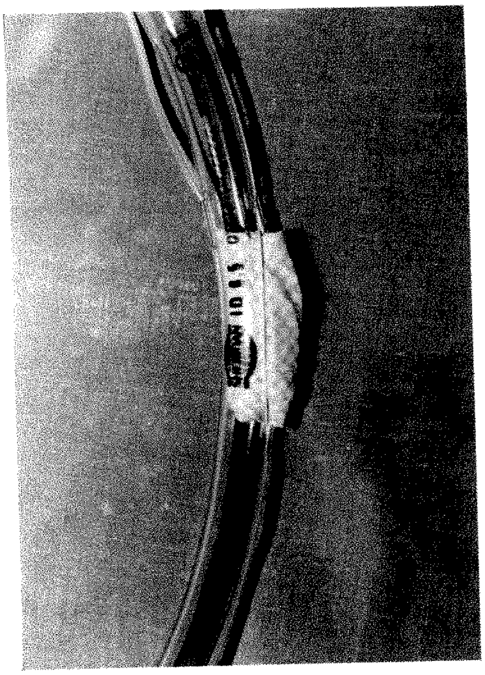


Fig. 1.

## Cryoanalgesia after thoracotomy

The conclusions in the recent comparison of thoracic epidural fentanyl infusion and intercostal nerve cryoanalgesia by J.D. Gough *et al.* (*Anaesthesia* 1988; **43:** 780–3) were interesting. It once again illustrates that cryoanalgesia does not provide adequate analgesia for the majority of patients who have a thoracotomy. We studied, in conjunction with Mr A.J. Gunning, the requirements for intramuscular opiate analgesia used alone and together with intercostal nerve cryoanalgesia in 12 thoracotomy patients, but abandoned the study on finding that the two groups had similar opiate requirements and similar perceived levels of pain. Very large numbers of patients would need to be recruited before any difference reached significance. However, the patients who had cryoanalgesia were often still complaining of hyperaesthesia and paraesthesia 2 or 3 years postoperatively. We returned to using high thoracic epidural analgesia with bupivacaine and recognised the increased demands for regular observation that this placed on the ward nurses. Epidural opiates were not routinely used because of the lack of suitable high dependency facilities. Cryoanalgesia continues to be used in many centres despite the, albeit restricted, availability of better methods and the continuing uncertainty about the morbidity it causes over subsequent years. A retrospective study of a large number of such patients would provide this information.

*John Radcliffe Hospital,*
*Oxford*
P.D. Cussons

## Spinal subdural haematoma after spinal anaesthesia

Dr Barker's report (*Anaesthesia* 1988; **43:** 664–5) of a subdural haematoma occurring after spinal anaesthesia was interesting. It is important that these events are made known to others, but we must be very careful in considering such unfortunate and, thankfully, very rare cases to be complications of spinal anaesthesia. The connexion between needle insertion and haematoma would seem causative, but lumbar puncture was atraumatic and the haematoma did not become apparent until a few days after the event. The haematoma could have been growing asymptomatically during that time, but it is important to remember that a similar case was reported in these pages in 1977 (*Anaesthesia* 1977; **32:** 78–9). The most important difference between the two cases was that the earlier patient received a general anaesthetic. Even if spinal anaesthesia can rarely cause such a lesion this shows that the use of general anaesthesia is no protection.

*The Royal Infirmary,*
*Edinburgh EH3 9YW*
J.A.W. Wildsmith

## Epidural fentanyl at 4°C for analgesia after epidural Caesarean section

Fentanyl was shown to be both a safe and effective analgesic when given by bolus or infusion into the epidural space after Caesarean section.[1,2] However, its short duration of action necessitates top-up or infusion techniques. These in turn may lead to delay in achieving analgesia, periods of no analgesia, or the need for more intensive nursing and monitoring, which all make the technique labour intensive for both medical and nursing staff. Epidural fentanyl causes plasma levels similar to those seen after an intramuscular injection. Plasma levels can be reduced by the addition of adrenaline (giving plasma levels similar to intravenous infusion), and thus decrease the side effects of sedation and dizziness. There is also a more rapid onset of analgesia because of decreased vascular uptake and hence an increase in this concentration gradient across the dura.[3] Boluses of 10 ml of normal saline at 4°C were shown to cool the epidural space to below 20°C for approximately 10 minutes;[4] this presumably produces epidural vasoconstriction for a similar length of time. Thus the use of cold epidural fentanyl might lead to a decrease in side effects and rapid onset of analgesia similar to the use of fentanyl with adrenaline. We investigated the effect of epidural fentanyl (100 μg 10 ml normal saline) cooled to 4°C on the speed of onset of analgesia as assessed by repeated visual analogue pain scoring, incidence of shivering, nausea, pruritus and sedation. We included ASA 1 and 2 patients undergoing elective Caesarean section under epidural anaesthesia, with 2% carbonated lignocaine only before the study.

We performed 14 injections on eight patients randomly allocated to 4°C or room temperature. The initial results (See Table 1) were so disappointing that the study was abandoned. The cold solution failed to provide adequate analgesia on three occasions. It tended to cause shorter duration analgesia and led to an increased demand on the anaesthetist; the patients were in pain more often and for longer. The nursing staff also noted that cold epidural fentanyl tended to wear off abruptly and completely and the patients were then in acute discomfort before the next dose of analgesic was given. No patients were shivering before the fentanyl injections and one patient shivered for 5 minutes after a cold injection. There was no incidence of nausea or sedation.

**Table 1.** Mean time in minutes (range) to achieve analgesia and duration of analgesia for cold (4°C) and room temperature epidural fentanyl.

| Time in minutes to: | Cold | Room |
|---|---|---|
| 50% reduction in pain score | 18.4 (6)** | 14 (9–24) |
| 75% reduction in pain score | 15 (9)** | 16 (9)* |
| Next analgesia | 111 (60–200) | 134 (45–278) |

** Three of the cold treatments failed to reduce the initial pain score by 50%.

* One of the room temperature treatments failed to reduce the initial pain score by 75%.

Cooling bolus doses of epidural fentanyl did not improve quality, speed or duration of analgesia after Caesarean section. Fentanyl has local anaesthetic properties[5,6] and perhaps our findings are not surprising in view of the effect of temperature on the onset time of local anaesthetics. We found the use of bolus fentanyl unsuitable for a busy clinical setting because of the short duration and rapidity with which epidural fentanyl wears off, and this practice has been abandoned.

*Foothills Hospital at*
*the University of Calgary,*
*1403 29th Street NW,*
*Calgary, Alberta,*
*Canada T2N 2T9*
M.J. Fairbrass
K. Jani
L. Strunin

### *References*

1. Madej TH, Strunin L. Comparison of epidural fentanyl with sufentanil. Analgesia and side effects after a single bolus dose during elective Caesarean section. *Anaesthesia* 1987; **42:** 1156–61.
2. Welchew EA. The optimum concentration for epidural fentanyl. A randomised, double blind comparison with and without 1:200 000 adrenaline. *Anaesthesia* 1983; **38:** 1037–41.
3. Henry M, Graizon A, Seebacher J, Vauthier D, Levron JC, Viars P. Epidural fentanyl with and without epinephrine plasma levels and pain relief. *Anesthesiology* 1988; **69:** A391.
4. Walmsley AJ, Giesecke AH, Lipton JM. Epidural temperature: a cause of shivering during epidural anesthesia. *Anesthesia and Analgesia* 1986; **65:** S164.
5. Power I, Brown DT, Wildsmith JAW. The effect of fentanyl on nerve conduction. *British Journal of Anaesthesia* 1988; **61:** 507P.
6. Gissen AJ, Gugino LD, Datta S, Miller J, Covino BG. Effects of fentanyl and sufentanil on peripheral mammalian nerves. *Anesthesia and Analgesia* 1987; **66:** 1272–6.

## Inadvertent cause of dural tap

Dr Valentine's letter (*Anaesthesia* 1988; **43:** 1062) on defects in epidural catheters, was interesting since I was involved with such a problem recently. An epidural was requested for a 28-year-old primigravida for analgesia during labour. The patient was of lean build and her spinous processes were easily identifiable. A 16-G Tuohy needle (Portex Minipack) was inserted into the epidural space at $L_{3-4}$ level, with the patient in the left lateral position. The corresponding catheter was then threaded through the needle, but resistance was felt when about 11 cm had passed through the hub of the needle.

Increased force of threading, followed by extension of the patient's hips proved to be of no value and so the needle and catheter were withdrawn together. On examination it was found that the cause of the obstruction was an apparent thickening of the catheter at 9.5 cm from the tip, which jammed against the end of the Tuohy needle, within the plastic hub, although the thickening was not obvious to the eye. A fresh needle and catheter were taken and inserted at the $L_{4-5}$ interspace with no problems. Good analgesia was obtained for the duration of labour and, after a failed forceps delivery, a healthy baby was eventually delivered by ventouse extraction.

The patient developed a mild frontal headache about 10 minutes after insertion of the first needle, but this did not inconvenience her, so she was closely observed throughout the postnatal period. Initially, the headache worsened, but since there had been no evidence of dural puncture, it was thought that this was probably unrelated to the epidural,[1] and the headache did, indeed, appear to resolve after 2 days. Six days after delivery her condition relapsed, and she now had a severe frontal headache, with neck stiffness and nausea unresponsive to parenteral metoclopramide therapy. There was no evidence of infection and so it was assumed that the symptoms were probably due to a concealed dural tap. The patient was rehydrated via an intravenous infusion for 24 hours and parenteral perphenazine prescribed as an antiemetic.

**Table 1.** External diameter of epidural catheter at varying distances from tip.

| Distance from tip of catheter (cm) | External diameter of catheter (mm) |
|---|---|
| 1.0 | 1.02 |
| 5.0 | 1.02 |
| 7.0 | 1.03 |
| 8.0 | 1.04 |
| 8.5 | 1.05 |
| 9.0 | 1.06 |
| 9.5 | 1.08 |
| 10.0 | 1.09 |
| 11.0 | 1.15 |
| 12.0 | 1.12 |
| 13.0 | 1.01 |
| 15.0 | 0.97 |
| 20.0 | 0.97 |

The next day, the nausea had resolved but the head and neck symptoms were unchanged, and so it was decided to perform an epidural blood patch. All symptoms disappeared within 20 minutes and the patient was able to stand and walk normally. She was discharged home the next day and has remained well since then.

The offending Tuohy needle and catheter were kept for more detailed inspection. The defect in the catheter was invisible to the naked eye, but a gradual bulge was detectable at 8 to 12 cm from the tip, under low power microscopy. Micrometry was then carried out to measure the external diameter of the catheter at various points (Table 1). The manufacturer's specifications state the external diameter of the catheter to be 1.1 mm.

The 16-G Portex epidural catheter is manufactured from radio-opaque nylon. Flexibility is minimal with the tip protruding 1 cm beyond the tip of the Tuohy needle, as occurred in this case, and the catheter acts like a short stylet. It is believed that, in performing the epidural, either excessive force upon the catheter or the movement of the patient in extending her hips was sufficient to perforate the dura mater, but this remained undetected since the needle was effectively blocked, and the catheter was not aspirated for cerebrospinal fluid.

It used to be necessary to check the compatibility of nondisposable needles and catheters in every case but I believed this to be unnecessary with modern, disposable equipment. This case leads me to reiterate Dr Valentine's suggestion that both needle and catheter should be tested for patency before their insertion.

*Cambridge Military Hospital,*
*Aldershot,*
*Hants GU11 2AN*

I.G. JOHNSTON

### *Reference*

1. MOIR DD, DAVIDSON S. Postpartum complications of forceps delivery performed under epidural and pudendal nerve block. *British Journal of Anaesthesia* 1972; **44:** 1197–9.

---

## Inadvertent paravertebral block

The use of newer nonionic contrast media to confirm the position of the epidural catheter and reveal inadvertent paravertebral placement as reported by Slappendel, *et al.* (*Anaesthesia* 1988; **43:** 939–42) can also be applied to confirm intentional thoracic paravertebral placement (Fig. 1).

We are also puzzled like the authors of the above-referenced work how 3 ml of local anaesthetic test dose, apparently deposited in a thoracic paravertebral space, could have produced bilateral sensory blockade. The catheter tip was perhaps placed in the extradural space close to an intervertebral foramen and a substantial percentage of the larger (8 ml) volume of contrast media diffused out into the paravertebral space as compared to the lower (3 ml) volume of the earlier local anesthetic injection.

Our experience with thoracic paravertebral block is not however similar to that of Conacher and Kokri.[1] We found that two out of three patients in a series of cases experienced bilateral sensory blockade after 30 ml 0.5% bupivacaine.[2,3] No patient who received 25 ml or less showed bilateral blockade. This effect was recently illustrated by a 41-year-old man with thoracic injuries who received an injection of 30 ml 0.5% bupivacaine in the right paravertebral space at $T_{6-7}$ level. Sensory loss was complete below $T_4$ on the right and below $T_{11}$ on the left side. Motor blockade occurred in the right lower extremity but there was no motor weakness on the left side. Twelve hours later a Burron* 18-gauge 9 cm Tuohy-Schliff needle was inserted in the right paravertebral space at the $T_{6-7}$

* Burron Medical Inc., 824 Tenth Ave., Bethlehem, PA 18018 USA.

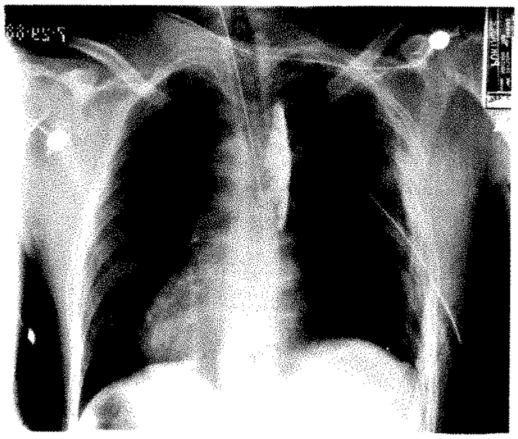


Fig. 1.

level and a 20-gauge polyamide catheter passed into the paravertebral space. A 0.22 micron filter was attached and the catheter position was confirmed by an injection of 3 ml iohexol 300 mg/ml. Injection of 25 ml 0.5% bupivacaine now produced only loss of pinprick sensation over a $T_{4-9}$ distribution on the right side. There was no loss of sensation on the left side and no motor blockade on either side.

We hope to report shortly on a series of patients treated with continuous thoracic paravertebral blockade, but in no patients studied to date, have we seen the distribution of local anaesthetic described by Conacher and Kokri.[1] Possibly the spread along the single intercostal space resulted from the presence of thoracic surgical incision thus reducing the effective volume in the paravertebral space. This may have led to their conclusion that 30 ml local anaesthetic failed to produce either clinical or radiographic evidence of contralateral neurological blockade.

In our two earlier cases it is possible that epidural blockade developed as suggested by Middaugh[4] but it could also be explained by spread across the anterior surface of the vertebrae as demonstrated by Mowbray.[5] Similarly the more recent patient who experienced unilateral lower extremity weakness with a 30 ml $T_{6-7}$ injection may have been experiencing lumbar plexus blockade rather than epidural blockade.

It appears that while small volumes of local anaesthetic injected into the paravertebral space are unlikely to produce bilateral sensory blockade, the phenomenon is quite common in our experience with 30 ml injections. The mechanism by which this bilateral blockade develops remains unclear.

*University of Texas,*
*Health Science Center,*
*San Antonio,*
*Texas 78284-7838,*
*USA*

J. GILBERT
S. SCHULEMAN
T. SHARP

*References*

1. CONACHER ID, KOKRI M. Postoperative paravertebral blocks for thoracic surgery. A radiological appraisal. *British Journal of Anaesthesia* 1987; **59:** 155–61.
2. GILBERT J. Thoracic paravertebral block—a method of pain control. *Critical Care Medicine* 1987; **15:** 445.
3. GILBERT J, HULTMAN J. Thoracic paravertebral block—a method of pain control. *Acta Anaesthesiologica Scandinavica* (in press).
4. MIDDAUGH RE, MENK EJ, REYNOLDS WJ, BAUMAN JM, CAWTHON MA, HARTSHORNE MF. Epidural block using large volumes of local anesthetic solution for intercostal nerve block. *Anesthesiology* 1985; **63:** 214–6.
5. MOWBRAY A, WONG KKS, MURRAY JM. Intercostal catheterisation. An alternative approach to the paravertebral space. *Anaesthesia* 1987; **42:** 958–61.

---

## Skin preparation and spinal headache

Dr Gurmarnik (*Anaesthesia* 1988; **43:** 1057) has drawn attention to the fact that not all headache after lumbar puncture may be due to leakage of cerebrospinal fluid. His list of the 'poisons' to be found in Betadine verges on the disturbing and I am quite sure that only small amounts of these are required in the cerebrospinal fluid to cause a chemical arachnoiditis. However, I am a little concerned that he felt it necessary to subject a considerable number of patients (with their consent?) to a clinical trial to demonstrate this. Very early in my medical career I was informed that this risk existed and taught that painting the skin with antiseptic should be virtually the first part of the procedure. The solution is left to dry (and exert its antiseptic effect) while I prepare everything required for the block and then wipe the area exposed by a fenestrated drape before doing anything else. The aim is that no liquid comes into contact with my hands or any of the equipment. It is not necessary to make more than one application of antiseptic and if it is washed off immediately with water even three applications will not have time to act.

*The Royal Infirmary,*
*Edinburgh EH3 9YW*

J.A.W. WILDSMITH

---

## Lignocaine 2% with adrenaline for epidural Caesarean section

We were interested to read the article by Norton, Davis and Spicer (*Anaesthesia* 1988; **43:** 844–9). Our experience with lignocaine 2% with adrenaline agrees with theirs.

We also use a freshly prepared solution with adrenaline in order to avoid the 0.1% sodium metabisulphite in commercially prepared solutions. Dr Norton and colleagues do not state which manufacturer's formulation of adrenaline they use to prepare their solution.

We prepare our solution from 20 ml plain 2% lignocaine to which is added 100 μg adrenaline immediately before injection into the epidural catheter. The measured pH of three sample solutions containing adrenaline (Evans Medical) was 4.86, and of three sample solutions containing adrenaline (Antigen) was 5.11. We contacted the manufacturers, and both preparations of 1:1000 adrenaline BP are made up in water for injection and contain 0.1% sodium metabisulphite. The pH of the Antigen solution is 3.5 (and of Evans Medical 3.6) on leaving the manufacturer. Evans Medical state an allowed drift to 2.8 by the end of the one-year shelf-life.

We suggest therefore that adrenaline nearing the end of its shelf life be avoided for epidural use. It is interesting that commercially available 0.5% bupivacaine with 1:200 000 adrenaline has a pH of 3.40 and is often used for epidural Caesarean section.

*John Radcliffe Hospital,*
*Oxford OX3 9DU*

D. BRIGHOUSE
O. DYAR

*A reply*

Thank you for the opportunity to reply. We are pleased to note that they share a similar experience in the use of freshly prepared 2% lignocaine with adrenaline solutions. The adrenaline used in our study was that produced by Antigen Limited.

It is stated that they also used freshly prepared solutions in order to avoid sodium metabisulphite. If adrenaline is added there is inevitably a low concentration (0.0005%) of sodium metabisulphite in 20 ml of lignocaine to which 0.1 ml of 1:1000 adrenaline is added. We, as stated clearly in our paper, wished to reduce the sodium metabisulphite concentration, but we recognise that it cannot be totally eliminated. Plain lignocaine 2% has little buffering capacity, so the addition of any adrenaline will result in a decrease in pH from the original solution. However, as Drs Brighouse and Dyar point out, there is a difference in the pH of freshly prepared lignocaine with adrenaline and commercially available 0.5% bupivacaine with adrenaline. If bupivacaine with adrenaline is to be used, alkalinisation with sodium bicarbonate appears to be a promising approach in reducing latency of onset and improving quality of analgesia.[1]

*University Medical Buildings,*
*Aberdeen AB9 2ZD*

A.C. Norton
A.G. Davis
R.J. Spicer

*Reference*

1. Tackley, RM, Coe AJ. Alkalinised bupivacaine and adrenaline for epidural Caesarean section. A comparison with 0.5% bupivacaine. *Anaesthesia* 1988; **43:** 1019–21.

---

## Tachyphylaxis and epidural anaesthesia

A 39-year-old primipara requested epidural analgesia early in labour; this was achieved without complications. She received intermittent top-ups of 8 ml 0.375% plain bupivacaine. The intervals between top-ups were 150–180 minutes. Labour became protracted and 29 hours after epidural analgesia was started it was decided to perform a Caesarean section for failure to progress. Towards the end of labour the top-ups were required at more frequent intervals and the three top-ups before operation were given at 25–30-minute intervals. She required a total of 35 ml 0.5% plain bupivacaine for a pain-free Caesarean section. She required, during the last 8 hours of the labour, a dose of bupivacaine of 2 mg/kg/hour; this is the maximum safe dose recommended. This patient had developed bupivacaine tachyphylaxis.

Tachyphylaxis is tolerance to a drug that develops rapidly after administration of only a few doses of that drug,[1] and is known to occur with amide-linked local anaesthetic agents. The mechanism of the development of tachyphylaxis to local anaesthetic agents was studied in dogs.[2] The lipid-soluble or nonionised form of the local anaesthetic is required to penetrate the cell membrane, and it is the ionised form that is required for its action upon or within the nerve cell. This study showed that repeated injections of acidic ionised local anaesthetic solutions into the intrathecal space causes the pH of the cerebrospinal fluid gradually to become acidic. This is because of the limited buffering capacity in this part of the body. Hence, less and less of the nonionised form becomes available. It may be assumed from this study that the epidural space also has a limited buffering capacity.

How should our patient's epidural analgesia have been managed, should her labour have continued? It was suggested that, to avoid tachyphylaxis during epidural analgesia, a high concentration of local anaesthetic with a long duration of action and a high pKa value be used.[3] This would favour bupivacaine as the agent of choice and perhaps indicate the 0.75% solution. However, this concentration is not available for use in the labour ward. The addition of adrenaline or dextran to the bupivacaine may prolong its action.

An alternative suggestion is to use a weak solution of local anaesthetic initially to effect analgesia.[4] Once the patient becomes refractory to this concentration, a stronger concentration of the same local anaesthetic may be used. This technique would favour a continuous infusion with a low dose concentration initially. A change to a different local anaesthetic agent was also suggested.[4] However, there is cross tolerance amongst the amide-linked local anaesthetic solution and a change to lignocaine would offer no particular advantage.

Justin and colleagues[5] have shown quite convincingly that the addition of fentanyl to bupivacaine prolongs the period between top-ups by about an hour. They reported no serious side effects other than itching in this study. This may be the best treatment for bupivacaine tachyphylaxis.

*Edgware General Hospital,*
*Edgware,*
*Middlesex HA8 0AD*

A. Ravalia
D. Browne
P.N. Robinson

*References*

1. Goodman and Gilman.—*The pharmacological basis of therapeutics*, 7th edn. New York: Macmillan 1985: 35–47.
2. Cohen EN, Levine DA, Colliss JE, Gunther RE. The role of pH in the development of tachyphylaxis to local anaesthetic agents. *Anesthesiology* 1968; **29:** 994–1001.
3. Doughty A. *Epidural analgesia in obstetrics. A second symposium.* London: Lloyd–Luke, 1980: 154.
4. Moore D. Regional Block. *A handbook for use in clinical practice of medicine and surgery*, 4th edn. New York: Thomas, 1975: 427–38.
5. Justins DM, Francis D, Houlton PG, Reynolds F. A controlled trial of extradural fentanyl in labour. *British Journal of Anaesthesia* 1982; **54:** 409–14.

---

## The distribution of drugs administered using the Bier's technique

Intravenous regional anaesthesia has been popular since 1963 when Holmes substituted lignocaine for the originally described procaine by Bier.[1,2] Raj and coworkers[3] came to the conclusion that the main sites of action are the peripheral nerve endings as well as the main nerve trunks in their study using X ray photography in conjunction with injection of radio-opaque solutions.

Our particular interest was in the distribution of injected solution in the skin during Bier's block. We devised an experiment to demonstrate the spread of a solution injected in a similar manner to a routine Bier's block. This involved injection of a dilute solution of methylene blue (25 mg in 40 ml saline) into a dorsal hand vein of a cuffed arm, exsanguinated with an Esmarch bandage. Changes in the colour of the skin were recorded with a video camera. The effect of the injection of the dilute methylene blue was that within one minute the antecubital fossa and discrete areas of the arm became blue. These same stained areas and elbow joint were associated with burning and aching pain, which necessitated removal of the cuff after only 2.5 minutes. The pain was treated with Bier's block with 0.5% prilocaine. The discoloration faded over 12 hours and the pain disappeared over the same time span. Methylene blue has a number of uses in clinical medicine. It can be used to treat methaemoglobinaemia since it is a reducing agent. It is also used surgically to assist in the delineation of certain glands such as the parathyroids. The recommended dose[4] is 5 mg/kg body weight although higher doses are given without causing any pain.[5] There are reports of local irritation of the urinary tract where the drug is excreted in high concentrations, and of irritation of the subcutaneous tissues when it is injected extravascularly.[6] We determined the weight of the arm by water displacement in a large measuring cylinder as 3.6 kg. The dose used was thus 7 mg/kg. High concentrations of methylene blue may have occurred locally within the arm that were difficult to predict, and this may have been a factor in the development of the observed pain. It would be interesting to know in conjunction with the present findings whether the degree of postoperative pain in parathyroid surgery is linked to the use of methylene blue.

*Guy's Hospital,*
*London SE1 9RT*

A.C. Beaumont
J. Gallagher
W. Hamann
J.R. Wedley

*References*

1. Bier A. Uber einen neuen Weg Localanasthesia an den Gliedmassen zu erzeugen. *Archiv für Klinische Chirurgie* 1908; **86:** 1007–16.
2. Holmes CM. Intravenous regional analgesia: a useful method of producing analgesia of the limbs. *Lancet* 1963; **1:** 245.
3. Raj PP, Garcia CE, Burleson JW, Jenkins MT. The site of action of intravenous regional anesthesia. *Anesthesia and Analgesia Current Researches* 1973; **5:** 776–86.
4. Dudley NE. Methylene blue for rapid identification of the parathyroids. *British Medical Journal* 1971; **3:** 680.
5. Blass N, Fung D. Dyed but not dead—methylene blue overdose. *Anesthesiology* 1976; **45:** 458–9.
6. Rhulen JL. Tissue necrosis. Cutaneous and subcutaneous damage following extravasation of methylene blue. *Journal of the Kansas Medical Society* 1982; **236:** 260.

---

## Further developments of the laryngeal mask

The author is indebted to Drs Brodrick, Webster and Nunn for their excellent paper (*Anaesthesia* 1989; **44:** 238–241) which is the first independent formal assessment of the laryngeal mask (LM) in its prototype form.

There are now four sizes (neonatal to large adult) and the introducer is no longer required.

The availability of larger sizes has also made it possible to ventilate the lungs at airway pressures up to 3.0 kPa in adults. It should be emphasised, however, that the LM offers no protection against aspiration of gastric contents. The trachea can be intubated blindly through the LM tube using an uncut 6-mm cuffed tracheal tube for LM sizes 3 and 4. This requires practice and the tracheal tube must be inserted with an approximately 15 degree left-hand rotation to avoid snaring of the bevel against the bars of the LM aperture. A well-lubricated tracheal tube can alternatively be gently inserted behind the partly deflated LM cuff into the upper oesophagus for gastric drainage. This manoeuvre can also be performed blindly. Either technique might perhaps be considered when tracheal intubation fails in the patient at risk.

Much work is still needed to assess the place of the LM in paediatric anaesthesia. The common practice of manual (forceful) bag-squeezing to check the position of a tracheal tube after insertion should never be used to check the position of the LM in adults or children. It is particularly inadvisable in children since it may result in rapid gastric distension even though the LM is correctly positioned. Positive pressure ventilation of the lungs is easily achieved with the LM in adults but there are insufficient data to recommend its use in paediatric anaesthesia at present.

The choice of induction agent when using the LM is influenced by the desirability of avoiding postoperative retching or vomiting and the need for quiescent laryngeal and pharyngeal reflexes during insertion. Inhalational induction in children and propofol in adults, both give excellent results in the author's own clinical experience when insertion is performed in the spontaneously breathing patient. If thiopentone is used, the patient needs to be deepened with a volatile anaesthetic before insertion is attempted.

*Newham General Hospital,*
*London E13 8RU*

A.I.J. Brain

---

## Use your Brain—to avoid stress?

We are interested to read the comments of Dr Alexander and his colleagues (*Anaesthesia*, 1988; **43:** 893–4) on the role of the Brain Laryngeal Mask (BLM) in anaesthetic practice. The authors claim the smoothness of cardiovascular responses to BLM insertion contrast markedly with the cardiovascular response to laryngoscopy and tracheal intubation. However, they supply no data to support this assumption.

A previous study found no difference in haemodynamic responses following tracheal intubation achieved by direct laryngoscopy or an indirect method.[1] In the light of this work, controlled studies which compare the pressor responses to BLM insertion with that of direct laryngoscopy and tracheal intubation are required. The authors' statement may be premature until such studies are undertaken.

*Newham General Hospital,*
*London E13 8RU*

R.M. Griffin
P. Dodd
G.C. Tosh
C. Buckoke

*Reference*

1. Knight RG, Castro T, Rastrelli AJ, Maschke S, Scavone JA. Arterial blood pressure and heart rate response to lighted stylet or direct laryngoscopy for endotracheal intubation. *Anesthesiology* 1988; **69:** 269–72.

## Laryngeal mask and patients with chronic respiratory disease

Brain's laryngeal mask airway, described as the missing link between the facemask and the tracheal tube, is used successfully in the management of difficult airways. Its use in day patients, thereby avoiding laryngeal penetration for minor head and neck surgery, is appreciated by many users of this convenient airway.

Personal experience with the use of laryngeal mask airway in 15 patients with chronic respiratory disease, (two with chronic obstructive airway disease, four with bronchial asthma and nine patients who smoked excessively) indicated some problems. Use of laryngeal mask airway in these patients provoked episodes of coughing, straining and bronchospasm unexpectedly during surgical anaesthesia. Six patients (smokers), one patient with chronic bronchitis and two asthmatics responded (60%) in this manner despite the fact that their respiratory problems were under control when they presented for surgery. It is known that these patients have hypersensitive respiratory reflexes.

Users[1,2] of this airway do not recommend the use of muscle relaxants or deep anaesthesia since the vocal cords and trachea are untouched. Thus this solution is not possible in the event of violent coughing and (or) bronchospasm.

An obese 53-year-old woman who smoked 40 cigarettes a day presented for a minor orthopaedic operation, after 20 mg temazepam orally as premedication. She tolerated a size 3 laryngeal mask airway well after induction of general anaesthesia with propofol and fentanyl, and was breathing a mixture of nitrous oxide, oxygen and 2% halothane. She developed, on transfer to the operating table, attacks of breath-holding which led to coughing, bronchospasm, and cyanosis. The laryngeal mask was difficult to remove despite the presence of a Guedel airway in order to administer oxygen because of rigidity of the jaw. Subsequently more propofol was given to allow the laryngeal mask to be removed. General anaesthesia was continued with nitrous oxide, oxygen and halothane and spontaneous ventilation without the laryngeal mask. Coughing and straining are likely at induction and during transfer. The laryngeal mask is difficult to remove quickly because of its size.

Patients with respiratory problems should not in my opinion be considered for the use of this airway for general anaesthesia and spontaneous ventilation.

*Barnet General Hospital,*
*Barnet,*
*Herts EN5 3DJ*
R.D. GUNAWARDENE

*References*

1. Brain AIJ. The laryngeal mask—A new concept of airway management. *British Journal of Anaesthesia* 1983; **55:** 801–5.
2. Alexander CA, Leach AB, Thompson AR, Lister JB. 'Use your Brain'. *Anaesthesia* 1988; **43:** 893.

## Cord examination after thyroidectomy

The vocal cords are routinely examined after a thyroidectomy before extubation to exclude damage to the recurrent laryngeal nerve.[1] Laryngoscopy, particularly at this juncture, can lead to violent straining and coughing which can contribute to reactionary haemorrhage. The view of the vocal cords is often far from satisfactory and so no comment can be made about their movement. Cord inspection can be made easily with the aid of a fibre bronchoscope. Once the muscle relaxants are reversed and normal ventilatory efforts return, 100% oxygen is introduced for 3 minutes. A fibre bronchoscope is then passed through the tracheal tube after pharyngeal suction. The tracheal tube is removed over the fibre bronchoscope and then the bronchoscope is also removed slowly and the cords are inspected as it is withdrawn. Cord movement could be seen without recourse to a further laryngoscopy in nineteen consecutive thyroidectomy patients.

*Pitea Lasarett,*
*941 28 Pitea,*
*Sweden*
V.J. SARMA

*References*

1. Atkinson RS, Rushman GB, Alfred-Lee J. *A synopsis of anaesthesia*, 9th edn. London: Wright, 1982: 371.

## On the insulation of needles

We have followed with interest the debate on the use of insulated and noninsulated needles for nerve block, carried out recently in the correspondence of this journal (*Anaesthesia* 1988; **43:** 167–8, 509, 991).

We would like to take issue with your last contributor, Dr Pither, on two points.

First, both his and Bashein's papers[1,2] could be seen as evidence in support of the preferred use of insulated needles with nerve stimulators but secondly and more practically with his statement that few hospitals have insulated needles.

We report here the simple means by which an insulated needle can be constructed swiftly and cheaply in any anaesthetic room in the country, assuming they have intravenous cannulae and all metal spinal needles.

We use the sheath of a Wallace 20-G intravenous cannula over a 22-G Needle Industries spinal needle and deliver the local anaesthetic through a Vygon Lectrocath. Various other combinations are possible including jamming the spinal needle into a narrow-gauge internal jugular cannula when a long needle is required, such as anterior approach to the sciatic nerve. Short-bevelled spinal needles are available if needed, but the essential ingredient is an all-metal spinal needle to which the crocodile clip of the nerve stimulator may be attached.[3]

*Northampton General Hospital,*
*Northampton NN1 5BD*
J. COLLIER
N.H. KAY

*References*

1. Ford DJ, Pither CE, Raj PP. Comparison of insulated and uninsulated needles for locating peripheral nerves with a peripheral nerve stimulator. *Anesthesia and Analgesia* 1984; **63:** 925–8.
2. Bashein G, Haschke RH, Ready LB. Electrical nerve location: numerical and electrophoretic comparison of insulated vs uninsulated needles. *Anesthesia and Analgesia* 1984; **63:** 919–24.
3. Koons RA. The use of the Block-Aid Monitor and plastic intravenous cannulas for nerve blocks. *Anesthesiology* 1969; **31:** 290–1.

## Propofol in acute porphyria

The case report by Weir and Hodkinson (*Anaesthesia* 1988; **43:** 1022–3) on the suitability of propofol for patients with porphyria raises some points which we consider require comment. The authors point out that the stress of surgery itself can produce an increase in the levels of urinary porphyrins. However, they do not consider the effect of kindling by any of these drugs subsequent to the alteration of porphyrin synthesis as a result of the stress of surgery.

The authors state, in the final paragraph, that none of the agents used in the final procedure are known to be porphyrinogenic. This is incorrect. The vocal cords were sprayed with 60 mg lignocaine which was shown to be porphyrinogenic in animal and cell culture models[1–3] and in data collected from clinical experience.[4] The use of this drug could mask any potential effect of propofol.

Thirdly, the authors have not mentioned whether or not other drugs were prescribed as premedication, as postoperative analgesia or for reasons unrelated to the surgical procedure, during the period of the 24-hour urine collection.

Finally, we have recently received the results of a prospective clinical trial of the use of propofol in patients with variegate porphyria.[5] This trial did not detect any adverse clinical or biochemical effects in 13 patients who had been given propofol. We consider that the authors have not presented a convincing argument against the use of propofol in patients with porphyria. Animal studies have suggested that propofol is not porphyrinogenic[6] and, until this report, propofol had been used in patients with acute porphyria uneventfully.[7–9]

*Royal Infirmary,*
*Glasgow G31 2ER*

M.J. McNeill
R.K. Parikh
M.R. Moore

*References*

1. Parikh RK, Moore MR. Effect of certain anaesthetic agents on the activity of rat hepatic d-Aminolaevulinate synthase. *British Journal of Anaesthesia* 1978; **50:** 1099–102.
2. Deybach J Ch, Da Silva V, Phung LN, Levy JC, Nordmann Y. Le risque medicamenteux des porphyries hepatiques. *Presse Medicale* 1987; **16:** 68–71. Drug risk of hepatic porphria. Development of an animal experiment model (English title).
3. Moore MR, McColl KEL, Rimington C, Goldberg A. *Disorders of porphyrin metabolism.* New York: Plenum Press, 1987.
4. *Riksforeningen mot Porfyrisjukdomar. Lakemedel som rapporteraats farliga vid akut intermittent porfyri, porphyria variegata ach hereditar koproporfyri.* Stockholm: Apoteksbolaget, 1985.
5. Meissner PN, Harrison GG, Kirsch RE. Diprivan (Propofol) as an intravenous anaesthetic induction agent in porphyria—results of a prospective clinical trial. Proceedings 'A Century of Porphyria': University of Glasgow 1989 (in press).
6. Parikh RK, Moore MR. A comparison of the porphyrinogenicity of di-isopropylphenol (propofol) and phenobarbitone. *Biochemical Society Transactions* 1986; **14:** 726–7.
7. Mitterschiffthaler G, Theiner A, Hetzel H, Fuith LC. Safe use of propofol in a patient with acute intermittent porphyria. *British Journal of Anaesthesia* 1988; **60:** 109–11.
8. Cooper R. Anaesthesia for porphyria using propofol. *Anaesthesia* 1988; **43:** 611.
9. McLougin C. Use of propofol in a patient with porphyria. *British Journal of Anaesthesia* 1989; **62:** 114.

*A reply*

Thank you for these comments on our case report. There will always be difficulty in determining the porphyrinogenicity of drugs used for anaesthesia in suceptible patients, because so many other stimuli (e.g. surgical stress, dehydration and other drugs) accompany their treatment. In response to the second point, I apologise, this should have read, 'none of the agents used in the final procedure have been shown to be porphyrinogenic in humans'.

Comment is not possible on the importance of the 60 mg lignocaine, used topically at the beginning of the 50-minute procedure, in causing the increase in urinary porphyrins. However, the patient had a similar procedure the day before under supraclavicular block, using 30ml 1.5% prilocaine without an increase in porphyrins. Neither premedication nor any known porphyrinogenic drugs in the postoperative period were given.

In all the clinical reports quoted by ourselves, and by the above authors, our report is the only one where propofol was given as continuous infusion over a long period. The patient described in our report received over 900 mg (more than twice any previously reported cases). The clinical reports (references 8 and 9, in the above letter), did not include measurements of porphyrins but state that there was no clinical evidence of adverse reaction, as was the case with our patient.

We gave our porphyric patient what we thought would be the least stimulatory anaesthetic and found to our horror that, although he had no clinical symptoms, his urinary porphyrins were markedly increased.

I look forward to the publication of the results of the prospective trial of propofol and variegate porphyria, but in the mean time will avoid the use of propofol (particularly in high dose) in patients with porphyria.

*Auckland Hospital,*
*Auckland,*
*New Zealand*

B. Hodkinson

## Fits after alfentanil and propofol

There are a few reports of fits after propofol. Epileptiform movements are described postoperatively or within seconds after the propofol injection.[1,2] Laycock suggests that fentanyl or alfentanil may potentiate the effect of propofol.[1]

We describe the case of a 71-year-old asthmatic and bronchitic man having a minor orthopaedic operation. He was on treatment with fenoterol and beclomethasone and consumed alcohol regularly. There was no history of convulsion or allergy. No premedication was given. An intravenous injection of 0.5 mg alfentanil was given, followed by the slow injection of 200 mg propofol (2.5 mg/kg). Approximately 15 seconds after the propofol, the patient developed strong bilateral fits and grimaces for 10 seconds, which must be described as epileptiform movements. Anaesthesia was maintained with $N_2O$, $O_2$ and halothane by facemask and spontaneous ventilation. There were no intra- or postoperative complications. It was the first time propofol had been given to this patient together with alfentanil.

Six months before the event the patient had the last of three anaesthetics in a short period, with propofol as the induction agent, without any problems. The patient was either premedicated or he received a muscle relaxant, which could have masked convulsive reactions in these three operations. Alfentanil was not used in any of these previous anaesthetics.

The pharmacokinetics of propofol during alfentanil anaesthesia gained recent interest.[3] Up to now, there is no clear evidence that alfentanil interferes with the disposition kinetics of propofol, but propofol may increase the plasma concentration of alfentanil.[3]

Our observation suggests that further consideration should be given to the possible association between epileptiform movements and the intravenous injection of alfentanil and propofol.

*Crawley Hospital,*
*Crawley,*
*West Sussex RH11 7DH*

U. WITTENSTEIN
D.J.R. LYLE

### *References*

1. LAYCOCK GJA. Opisthotonos and propofol: a possible association. *Anaesthesia* 1988; **43:** 257.
2. ICI-Pharmaceutical information service. Personal communication, November–December 1988.
3. GEPTS E, JONCKHEER K, MAES V, SONCK W, CAMU F. Disposition kinetics of propofol during alfentanil anaesthesia. *Anaesthesia* 1988; **43** (Suppl.): 8–13.

## Delayed allergic response to propofol

We wish to report a delayed allergic response to propofol. The patient was a fit 31-year-old man, who was admitted as a day case for removal of a wire from his right patella.

He had received a general anaesthetic 19 months previously for internal fixation of a right patellar fracture. The following drugs were used: thiopentone, fentanyl, atracurium, halothane, nitrous oxide, oxygen, glycopyrronium, edrophonium, papaveretum, metoclopramide and erythromycin. He was known to be allergic to penicillin which produced a skin rash. There were no complications with this anaesthetic.

The patient was not premedicated on this occasion and 200 mg propofol and 0.05 mg fentanyl was used for induction. Maintenance was with nitrous oxide, oxygen and halothane. Glycopyrronium was given for bradycardia.

The operation lasted 35 minutes. The patient awoke rapidly and the first 40 minutes of recovery were uneventful. He then began to complain of difficulty in breathing and in swallowing. His face, especially the lips and eye lids, became swollen. There was inspiratory stridor, expiratory wheezing, peripheral cyanosis and cold, clammy skin. Pulse rate was 120 per minute and arterial blood pressure 80–60 mmHg.

He was then given 100 mg hydrocortisone and 10 mg chloropheniramine intravenously. His condition deteriorated and he was given 400 mg thiopentone and 100 mg suxamethonium to enable a 9.0-mm cuffed tracheal tube to be passed. There was moderate laryngeal oedema.

His lungs were ventilated for an hour and he was also given midazolam 5 mg and atracurium 15 mg. He was well enough to be exubated at the end of this time. The bronchospasm resolved after 2 hours and the facial swelling was gone by the next day.

He was discharged in good condition on the third day. Blood samples were taken 2, 10 and 22 hours after the onset of the symptoms. There were no abnormalities of immunoglobulins (IgG, IgA, IgM, IgE) and complement levels were normal; on the basis of this, propofol seems a more likely cause of the reaction than fentanyl or any other drug. It is possible that this was a prostanoid reaction, which may occur in the lungs of susceptible patients.

We suggest that whenever propofol is used for daycase surgery, patients are not discharged from hospital for at least 2 hours. This is especially important for patients with a confirmed history of drug allergy.

We are very grateful to Dr J. Watkins of the Department of Immunology at the Royal Hallamshire Hospital for his help with the blood tests and his advice.

*District General Hospital,*
*Colchester CO4 5JL*

M. DOLD
W.H. KONARZEWSKI

## The use of ketamine in civilian and military surgery

We read with great interest the article by Restall *et al.* (*Anaesthesia* 1988; **43:** 46–9). The article reveals a plausible and useful anaesthetic technique, which was used and published before, with diazepam instead of midazolam and the title may be somewhat misleading.

First of all, the authors attempt to extrapolate their data to an entirely different situation. Elective operations were performed in their study on healthy ASA Class 1 and 2 patients, instead of victims of trauma from battle or otherwise. The patient characteristics would then be entirely different in the two groups and with different values. Extrapolation from a purely elective study to battle casualties is at best very difficult.

The authors' statement that, 'the cardiovascular system is supported in the treatment of hypovolaemic battle casualties and that blood pressure does not decrease after induction', if ketamine were used, is not entirely correct and readers of the article may be misled.

Lippmann, *et al.*[1,2] have published several articles, with ketamine as the induction agent, which show that ketamine causes hypotension and not hypertension in hypovolaemic and debilitated poor risk patients, some of whom were trauma cases. Naturally, as the authors mentioned, 'maintaining blood pressure or increasing same in hypovolaemic battle casualties would be beneficial' goes without saying, but that is not always the case. Hypotension with reduced cardiac output does occur and may be profound and anaesthetists must be aware of this effect when ketamine is used as an induction agent.

The use of benzodiazepines to ameliorate postoperative ketamine-induced mental abnormalities and to afford amnesia is well-known. To use this type of drug (diazepam or midazolam) in elective healthy individuals is one thing, but in battle casualties could lead to increased morbidity and mortality. Diazepam has been shown to have undesirable effects, especially on arterial blood pressure which decreases. Midazolam, which is more potent than diazepam will depress ventilation even more. Hypotension, due to its myocardial effect, may occur in severely wounded battle casualties and therefore it may not be the drug to use. Correction of mental aberrations would be the least of our worries.

Ketamine, compared to thiopentone or other intravenous myocardial depressant agents, may still be the anaesthetic of choice for induction of anaesthesia. However, anaesthesiologists world wide must be aware of its adverse effects.

*University of California Los Angeles,*
*Medical Center,*
*Torrance, California 90509*
*USA*

M. LIPPMANN
D. HSU

*References*

1. WAXMAN K, SHOEMAKER WC, LIPPMANN M. Cardiovascular effects of anesthetic induction with ketamine. *Anesthesia and Analgesia* 1980; **59:** 355–8.
2. LIPPMANN M, APPEL P, MOK MS, SHOEMAKER WC. Sequential cardiorespiratory patterns of anesthetic induction with ketamine in critically ill patients. *Critical Care Medicine* 1983; **ii:** 730–4.

*A reply*

Thank you for giving us the opportunity to reply to Dr Lippmann's letter and we are grateful for his comments.

It is difficult to extrapolate the results from a series of 100 elective cases to the battle casualties for which the technique was designed. Ethically it is hard to recruit trauma victims into a study. The alternative is a series of anecdotes from a war zone. Our patients would be men and women with normal cardiorespiratory functions before injury. Battle injury is an acute insult to a previously fit individual. The 12 patients studied by Waxman *et al.*[1] were severely debilitated by a chronic disease process and many were in a state of septic shock.

We accept that ketamine may produce hypotension in the order of 10% on induction. However this is significantly less than that produced by any other induction agent. Hypotension which results from ketamine and midazolam is reversed by the haemodynamic response to tracheal intubation.

We defend the use of midazolam. Certainly it is more potent that diazepam and therefore it is important that the dose we recommend is not exceeded. It is most unlikely that these doses of midazolam will have any adverse effect on morbidity or mortality. We believe that hallucinations during recovery can be a serious problem. The concurrent use of low dose ketamine and low dose midazolam have totally abolished psychomimetic phenomena.

We do not claim to have discovered anything totally new; a similar combination of drugs had been described before.[2] We have used this technique very successfully and safely in victims of road traffic accidents, gunshot wounds and bomb blast. We have tried to describe an intravenous, as opposed to an inhalational, method for general anaesthesia for trauma cases in the Field. No method can be 100% safe but we believe that our method is safer than most. If any reader has a safer method for anaesthesia in a hostile environment we should be happy to hear about it.

*Cambridge Military Hospital,*
*Aldershot,*
*Hants GU11 2AN*

J. RESTALL
A.M. TULLY
P.J. WARD
A.G. KIDD

*References*

1. WAXMAN K, SHOEMAKER WC, LIPPMANN M. Cardiovascular effects of anesthetic induction with ketamine. *Anesthesia and Analgesia* 1980; **59:** 355–8.
2. WHITE PF. Comparative evaluation of intravenous agents for rapid sequence induction—thiopental, ketamine, and midazolam. *Anesthesiology* 1982; **57:** 279–84.

## Perished latex

We report a hazard associated with the use of the Venisystems, extension set with 'T' when used as a connecter to an arterial cannula.

The usual method of connecting an arterial cannula to the transducer manometer tubing in this department is by means of the extension set described above (care is taken to make a firm connexion in view of the lack of a luer lock). This provides a small and convenient connector with a rubber port from which arterial blood can be sampled close to the cannula. A brisk leak of arterial blood from the extension set was noticed in a recent case while the patient was positioned on the table. Closer examination showed that the rubber port had disrupted under arterial pressure due to perishing of its rim. The extension set was within its expiry date, and was stored in a dry environment at room temperature. Examination of another set revealed similar perishing, well within the expiry date.

We suggest that this type of extension set be examined closely for perishing especially if it is to be used in arterial monitoring and subject to pressure. The arterial cannula and extension set should not of course be concealed by drapes.

*Southampton General Hospital,*
*Southampton,*
*Hants SO9 4XY*

D.N. SUTTON
V.L. THOMAS

*A reply*

We are very concerned to hear about Dr Sutton's experience with one of our Venisystem Extension Set, with 'T' units. However, Abbott Venisystems are designed and intended for use under venous pressures only and luer lock is available. If the system were connected to a pressure transducer, the tracing would be damped. There have been a few reported instances of discoloration of the latex injection site, but resultant performance is satisfactory.

However, in line with our policy of continued product improvement, the formulation of the latex used in this product was modified in order to overcome the problem of its appearance.

We would like to assure your readers that Abbott has a continuing commitment to provide the highest quality products fully suited to their intended use.

*Abbott Laboratories Ltd,*
*Queenborough,*
*Kent ME11 5EL*

K. DOBSON

## $CO_2$ measurement and the Minilink system

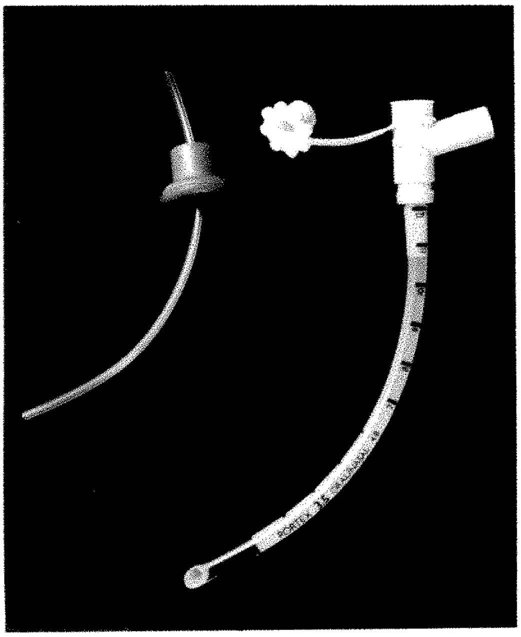


**Fig. 1.** $CO_2$ Sampling system with the Portex 8.5/6-mm Minilink connector, Drager bung, and Datex $CO_2$ sampling tubing.

The recent letter from Reid and Matthews about measurement of $CO_2$ using readily available disposable equipment (*Anaesthesia* 1988; **43:** 902–3), prompts us to describe a system that we have used at our hospital for several months. We have devised a system using a flexible flanged bung that is found on Drager disposable paediatric ventilator tubing, or can be ordered separately (order code 8402953). This bung fits snugly over the top of the Portex 8.5/6 mm tube connector and through which we insert the Datex $CO_2$ monitoring tubing (Fig. 1).

The system enables analysis of gas from any part of the tracheal tube and allows accurate $CO_2$ measurement,[1] if the length of monitoring tubing inside the tracheal tube is varied. We have found this system highly satisfactory; it adds little bulk or height to the catheter mount, and is very easy and cheap to use. The sampling tubing can be wiped with alcohol between cases, shortened or thrown away.

*Guy's Hospital,*
*London SE1 9RT*

A.C. BEAUMONT
J.G. DIAMOND

*Reference*

1. BADGWELL JM, MCLEOD ME, LERMAN J, CREIGHTON RE. End-tidal $P\mathrm{co}_2$ measurements sampled at the distal and proximal ends of the endotracheal tube in infants and children. *Anesthesia and Analgesia* 1987; **66:** 959–64.

---

## Another use of the pulse oximeter

We would like to present another use for a pulse oximeter. A papaveretum infusion was inadvertently connected to an arterial line in the left radial artery. The infusion was in progress for approximately 3 hours before discovery and the patient received 20 mg papaveretum of a solution containing 1 mg/ml saline.

On discovery the arm was cyanosed ($S\mathrm{ao}_2$ 50%) cold, brawny, oedematous and painful. The patient refused both a stellate ganglion block or brachial plexus block and therefore 10 mg papaverine hydrochloride in 10 ml of 0.9% NaCl was given via the indwelling cannula into the affected artery. This resulted in immediate improvement in blood flow to the hand as shown by an improvement in colour, temperature, and oxygen saturation to 98%. The arm was elevated in a Brook Sling (a roller towel over a drip stand with the arm flexed at 90° at the elbow) with an oximeter constantly monitoring the oxygen saturation. Twelve hours later the oxygen saturation decreased to 70%. Perfusion was again improved by the intra-arterial injection of 10 mg 0.1% papaverine hydrochloride. Oxygen saturation returned to 98% and remained at this level thereafter.

The increasing use of both intravenous infusions and arterial lines means that this accident is likely to occur again. We think that this case demonstrates a further use of the pulse oximeter.

*Royal National Orthopaedic Hospital,*
*Stanmore,*
*Middlesex HA7 4LP*

L. MURDOCH
A. BRAY

---

## A useful tip

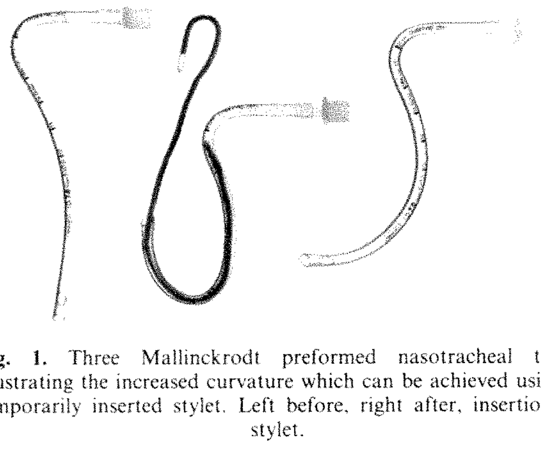


**Fig. 1.** Three Mallinckrodt preformed nasotracheal tubes illustrating the increased curvature which can be achieved using a temporarily inserted stylet. Left before, right after, insertion of stylet.

The use of Mallinckrodt preformed nasotracheal tubes greatly facilitates surgical access during dental operations. However, these tubes tend to be rather less curved than either the plain disposable or red rubber varieties, while the bend at the nose and the added length make it difficult to insert and withdraw a stylet in the conventional manner. The tip of the tube may as a result, damage structures on the posterior pharyngeal wall, and subsequently it may be difficult to pass the tube anteriorly through the larynx.

One way of providing the tube with greater curvature and a 'ski tip', is to introduce a stylet temporarily via its *tracheal* end and bend it into a J shape (see Fig. 1). The stylet can be withdrawn after 15–20 minutes leaving the tube sufficiently curved to facilitate nasal intubation.

*Royal Manchester Children's Hospital,*
*Pendlebury,*
*Manchester M27 1HA*

G. MEAKIN

## Failure of rectal diclofenac to augment opioid analgesia

The study by Colquhoun and Fell (*Anaesthesia* 1989; **44:** 57–60) was interesting.

My preliminary results, which were presented in abstract form at the Anaesthetic Research Society,[1] are now fully analysed.

Healthy women about to undergo major gynaecological surgery were studied. Twenty-two patients received diclofenac 50 mg orally with premedication and 100 mg rectally in the recovery area in a randomised double blind study, which had local ethics committee approval, and for which subjects gave informed consent. Twenty-one received matched placebo medication.

The amounts of papaveretum given in the recovery area as required on a normal basis were recorded. Patients who had received diclofenac premedication received a mean of 6 mg papaveretum (range 0–20 mg), while the placebo-treated group received a mean of 8 mg (range 0–20 mg); 18.6 mg(range 0–35 mg) and 24 mg (range 0–45 mg) were given in the next 12 hours respectively. Thus the diclofenac-treated group received 24.6 mg papaveretum and the placebo-treated group 32 mg in the immediate period after operation. The amounts of papaveretum administered to each group were similar in the second 12-hour period (19.7 mg and 18.8 mg respectively).

The amount of papaveretum administered to each group differs by over 14.7%, but this is not statistically significant. The method is crude, but for a new technique to be accepted, the benefits should be obvious.

However, re-analysis of the results (Table 1), suggests that pre-operative NSAID may be of value. (Chi squared = 4.04; $p < 0.02$).

**Table 1.** Number of patients in each group who received papaveretum (before the suppository).

| | 0–10 mg | 10.1–20 mg |
|---|---|---|
| Diclofenac | 17 | 5 |
| Placebo | 10 | 11 |

Two points are worthy of note. Firstly some diclofenac was also given before operation so that the nonsteroidal could work before surgery. Secondly, the dose of 50 mg was limited by the 100 mg suppository formulation available at the start of the study, coupled with the manufacturer's recommendation of a maximum dose of 150 mg daily.[2]

Subsequently the manufacturers informed me (personal communication) that the 150 mg maximum daily is recommended for *chronic* administration. Larger doses might be free of the long term sequelae in acute administration. It is my practice now to administer more and earlier NSAID.

*Warwick Hospital,*
*Warwick CV34 5BW*
D.R. DERBYSHIRE

### *References*

1. DERBYSHIRE DR, RICHARDSON J. Voltarol (diclofenac) as a perioperative analgesic supplement. *British Journal of Anaesthesia* 1987; **59:** 1327P–8P.
2. Data Sheet Compendium. London: Datapharm Publications, 1988.

---

## Potential hazard with Graseby PCAS

The Graseby PCAS (patient controlled analgesia system) is a modification of the MS 2000 infusion pump with the necessary additional programming facilities and security features required for this operation.

In order to set the drug administration parameters a key must be inserted and turned 90° clockwise to switch the PCAS from the 'off' to the 'reprogram/unlock' position. Reprogramming can now take place and a security bar can be opened to gain access to the syringe.

Once reprogrammed *two* further manoeuvres are required to activate PCAS. The key must be turned a further 90° clockwise to the 'on' position and the 'run' button pressed.

It has become apparent to us that this second step is not only required to start PCA but is the manoeuvre which isolates the reprogramming facility. Thus, if the security key is turned to 'on' and removed from the pump but the 'run' button is not pressed, either by omission or after a conscious decision to defer starting PCA, then it is still possible for any unauthorised person, either deliberately or accidentally, to alter the settings of bolus dose or infusion rate.

The likelihood of this is impossible to assess. It can be lessened by an awareness of the problem among staff using the PCAS but the wider general acceptance of patient-controlled analgesia depends, among other things, on these potential hazards being recognised and eliminated.

*John Radcliffe Hospital,*
*Oxford OX3 9DU*
S.F. JONES
M.K. REEDER

---

## Antipollution of the future

Taking care of the environment means throwing rubbish across the garden fence, dumping waste into the sea, or pumping gases into the atmosphere. This is the standard we have so proudly achieved with our antipollution systems in theatres. The anaesthetic vapours do form only a very small part of the global problem, but they are dumped there by us, a group of people who should know better and, in fact, can do better. The technology is there and the answer is recycling.

We used charcoal adsorption to remove halothane from the exhaled gases only a few years ago. Halothane is cheap and economic extraction could be hard to achieve. The problem of low cost is no longer there with the new agents, especially isoflurane.

Isoflurane can also be adsorbed on charcoal and one presumes that, for example, gentle heating would release practically unchanged isoflurane in a very pure form at minimal cost. There should be a profit for the enterprising chemist or even for the manufacturers. Is there a hidden reason why this can not be done?

*Princess Alexandra Hospital,*
*Harlow,*
*Essex CM20 1QX*
Z. ZYCH

*Anaesthesia*, 1989, Volume 44, pages 537–538

# Book reviews

**Anaesthesia at the district hospital** 537
M.B. Dobson
**A tribute to Professor Sir Robert Macintosh for his 90th birthday** 537
Edited by W.D.A. Smith and G.M.C. Paterson
**Clinical anatomy for anesthesiologists** 537
R.S. Snell and J. Katz
**Anesthesiology report Vol. 1, No. 1** 538
Edited by M.C. Rogers, R.C. Wetzel, E.D. Miller, Jr. and W.D. Watkins
**Books received** 538

### Anaesthesia at the district hospital

M.B. Dobson. Pp. 143. World Health Organization, 1988. $16.00.

This book is aimed at the nonspecialist practising anaesthesia in the first referral hospitals in the Third World with limited equipment, drugs and personnel. It aims to provide such practitioners with a practical guide to the provision of safe and effective anaesthesia under just these conditions and generally succeeds.

The reader is guided from pre-operative assessment and preparation of the surgical patient, through induction and maintenance of anaesthesia, to recovery and postoperative care. Medical conditions and the anaesthetist, intravenous fluid therapy and care of the critically ill or injured are well covered. There are also brief descriptions of general anaesthetic drugs and anaesthesia for paediatric and obstetric patients. The step-by-step account of specimen general anaesthetic techniques should cover most situations arising in the district hospital. The informative chapter on conduction anaesthesia, though far from comprehensive, includes the blocks of most use to the anaesthetist with limited equipment and expertise. The description of apparatus for inhalation anaesthesia is first class. The author correctly concentrates on drawover systems, highlighting their inherent safety and suitability for the isolated unit. The setting-up and testing of various systems utilising available components, is clearly described and there are useful notes on simple maintenance and sterilisation of equipment.

Information is presented in a clear and concise form with excellent uncluttered illustrations to complement the text and an adequate index. The book is intended for the nonspecialist, so its content is rather elementary with the emphasis on safety and practical procedures. The golden rules and guidelines for safe practice quoted here should, if followed, keep most anaesthetists out of trouble. Obviously such a book cannot be comprehensive but I was surprised to find no mention of absorption systems, management of the emergency thoracotomy, anatomy of central venous access and Apgar scoring of the neonate. The pharmacology of anaesthetic drugs and the uptake and distribution of inhalation anaesthetic agents surely deserve more extensive explanation.

In summary, with these minor reservations, I found this to be an excellent, accurate, basic manual. When read in conjunction with practical training under specialist anaesthetists it should equip the probationer to approach the provision of safe anaesthesia in the remote hospital with confidence. One hopes that the book's simple style will attract other readers among his medical and nursing colleagues as the admirable accounts of resuscitation and preparation of the patient for surgery deserve wide circulation.

A.K. Scott

### A tribute to Professor Sir Robert Macintosh for his 90th birthday

Edited by W.D.A. Smith and G.M.C. Paterson. Pp. 40. RSM, 1988. £7.95.

On 2 October 1987, a joint meeting under the auspices of the Section of Anaesthetics of the Royal Society of Medicine, The Association of Anaesthetists of Great Britain and Ireland, and the Faculty of Anaesthetists of the Royal College of Surgeons of England was held at the Royal Society of Medicine to pay tribute to Professor Sir Robert Macintosh on the occasion of his 90th birthday (17 October 1987); Professor Keith Sykes took the chair.

This slim volume is a verbatim transcript of the proceedings. It is not a Festschrift nor is it a history of the Nuffield Department of Anaesthetics, Oxford—a subject which was recently dealt with fully in Jenny Beinart's Golden Jubilee Book of the Department. It is a collection of seven contributions by past and present members of the Department each one dealing with a single sphere of Sir Robert's interest in and contribution to anaesthesia.

To attempt to cover such a wide field in the space of a bare hour, ruthless and arbitrary selection of these topics was obviously essential. The final choice covered his contributions to academic anaesthesia, physics, drawover and local anaesthesia, and the introduction of anaesthetic nurses. The other two presentations covered the period after Sir Robert's retirement and his very close bonds with the Section of Anaesthetics of the Royal Society of Medicine. One recurring theme runs clearly through all these papers—the deep and genuine affection in which 'Mac' was held by all who worked with him at any time or in any way. Perhaps one's only regret might be that there was little or no clear exposition of his role as the 'father of many departments' through his first assistants who moved on to found other premier anaesthetic establishments. This book is a unique record and memento of a unique occasion on which tribute was paid to a unique man.

P.W. Thompson

### Clinical anatomy for anesthesiologists

R.S. Snell and J. Katz. Pp. 328. Appleton and Lange, 1988. £77.00.

Professors Snell and Katz have written a good theoretical clinical anatomy book. They cover all the main systems of interest to the anaesthetist in the nine chapters.

The first two chapters give an excellent overview of the respiratory system, but the electron micrographs, radiographs and CT scans that they contain add little to the text. The following chapters describe in turn: the cardiovascular system, the vertebral column, the spinal cord, the peripheral nervous system and the cranial nerves. The final two chapters summarise the anatomy of the autonomic nervous system, the perception of pain and the control of muscular activity. These last subjects are often covered only briefly in anatomy textbooks, but here they have been dealt with clearly and in detail.

There are 'clinical notes' in each chapter which, although they often say less about the anatomy of a clinical problem than many standard anaesthetic or surgical textbooks, add interest to what many may regard as a dry subject. Each chapter ends with a number of clinical problems and asks for the anatomical explanation; a useful exercise for examination purposes.

The text is clear and, as a reference book, succinct. It is interspersed with a large number of illustrations. Many are very clear but some are difficult to interpret: sketched line drawings, poorly orientated and inadequately labelled. The lack of high quality colour drawings is a striking omission in a book of this price.

The anatomy of all the commonly used nerve blocks is covered, with the exception of that of the penis, and nerve block techniques are described in the clinical notes sections. The book is not, however, a textbook of regional anaesthesia and cannot be used as such.

It is excellent as a reference book for the anaesthetist who wants to know the anatomical answer, and would be a useful addition to any departmental library. It is perhaps too expensive and too detailed as a textbook for the anaesthetist who is studying for the first or third part of the postgraduate examination but it is still very easy to read and covers all the anatomy of likely interest to the examiner.

M.H. CROSS

### Anesthesiology report Vol. 1. No. 1.

Edited by M.C. ROGERS, R.C. WETZEL, E.D. MILLER JR. AND W.D. WATKINS. Pp. 145. C.V. Mosby, 1988. $55.50 for three issues a year.

*Anesthesiology Report* is yet another addition to the growing number of review journals aimed at a periodic update of our skills and knowledge. The level is fairly specifically pitched at the American clinical anesthesiologist, and American styles of practice. The first issue is devoted to paediatric anaesthesia, which of its nature is prone to parochial dogma, and the articles here are no exception, liberally spiced with 'we recommend' and 'x is contraindicated'. These aphorisms are frequently extracted from the text and highlighted in coloured tablet form, presumably for those who do not wish to read the rest. This is a pity, because the magazine format, and the high quality of illustrations makes this journal easy to read.

There is an excellent summary of the difficult topic of paediatric cardiopulmonary resuscitation, which is of general interest to all anaesthetists, and an article relating the illuminating range of outpatient procedures prevalent in the USA, which would make most of inpatient paediatric surgery in UK redundant. There are two comprehensive articles on individual techniques for major reconstructive surgery for congenital deformities, and a well constructed case report of the common neonatal problem of anaesthesia for the surgery of necrotising enterocolitis. The case report illustrates, however, the difference in transatlantic practice, with the authors agonising over optimal oxygen concentration during surgery, while delegating postoperative care to some other group of doctors.

For the casual reader, therefore, this issue was an interesting insight into the way that American paediatric anaesthesia is going, and to what we have to learn from them. The development of the subspecialty is dealt with in detail in the editorial. To become a subscriber, one would be looking for a journal with 'how-to-do-it' reviews as an alternative to frequently updating basic textbooks. However, with only three issues each year it is not likely that it could cover the whole range of clinical practice in a fast enough cycle. There are very few references for a review journal (approximately 140 in this issue) and hardly any from non-American journals, this despite a glowing testimonial in the editorial for the major contribution of UK workers in this field.

In fairness, the first issue of a new periodical could either reflect initial flair, or small beginnings and I await developments, preferring in general the more studious approach adopted by *Seminars in Anesthesiology*.

D.E.F. NEWTON

## Books received

We thank the publishers for the following books, some of which may be reviewed in future issues of the journal.

**Bailliere's Clinical Anaesthesiology Vol. 2, No. 2. Some aspects of anaesthetic safety**
Guest editors O.P. DINNICK AND P.W. THOMPSON. Pp. x + 441. Baillière Tindall, 1988. £15.00.

**Cardiovascular anesthesia and postoperative care, 2nd edn.**
Edited by S. TARHAN. Pp. xviii + 651. Year Book Medical, 1988. £59.50.

**Pharmacolgie en pratique anesthésique, 2nd edn.**
P. DUVALDESTIN. Pp. ix + 269. Masson, 1989. F289.

*Anaesthesia*, 1989, Volume 44, pages 539–544

# Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for February 1989. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

## Abdominal surgery

Kinins as mediators of intestinal secretion. Gaginella TS, Kachur JF. *American Journal of Physiology* 1989; **256** (No. 1 Part 1): G1.

## Pharmacology

### *Adrenergic drugs and their antagonists*

Cardiovascular responses to metipranolol and timolol eyedrops in healthy volunteers. Bacon PJ, Brazier DJ *et al. British Journal of Clinical Pharmacology* 1989; **27:** 1.

Propranolol increases prostacyclin synthesis in patients with essential hypertension. Beckmann ML, Gerber JG *et al. Hypertension* 1988; **12:** 582.

Pharmacokinetics of non-prescription sympathomimetic agents. Chua SS, Benrimoj SI, Triggs EJ. *Biopharmaceutics and Drug Disposition* 1989; **10:** 1.

Beta-adrenergic receptor function and oxygen radical production in bovine pulmonary alveolar macrophages. Conlon PD, Ogunbiyi PO *et al. Canadian Journal of Physiology and Pharmacology* 1988; **66:** 1538.

SK and F 86466, a novel alpha-adrenolytic drug: effects on heart rate, BP and neuroendocrine function in supine resting position and in response to postural and cold stimulation in normal humans. De Mey C, Enterling D *et al. Journal of Cardiovascular Pharmacology* 1989; **13:** 25.

Differences in beta-blocking drugs in cardiovascular therapy. Iisalo E, Heikkila J *et al. Annals of Clinical Research* 1989; **20:** 324.

Studies on the mechanism of prazosin induced sympathoinhibition. Ito T, Hey JA, Koss MC. *European Journal of Pharmacology* 1988; **158:** 225.

Therapeutic applications of drugs acting on alpha-adrenoceptors. Macdonald E, Ruskoaho H *et al. Annals of Clinical Research* 1988; **20:** 298.

Comparison of respiratory effects of two cardioselective beta-blockers, celiprolol and atenolol, in asthmatics with mild to moderate hypertension. Vanzyl AI, Jennings AA *et al. Chest* 1989; **95:** 209.

### *Anaesthetic agents*

Effects of low levels of $NO_2$ on terminal bronchiolar cells and its relative toxicity compared to $O_3$. Chang L-Y, Mercer R *et al. Toxicology and Applied Pharmacology* 1988; **96:** 451.

Hormonal responses to analgesic nitrous oxide in man. Gillman MA, Katzeff I *et al. Hormone and Metabolic Research* 1988; **20:** 751.

Intravascular mixing and drug distribution: the current disposition of thiopental and indocyanine green. Henthorn TK, Avram MJ, Krejcie TC. *Clinical Pharmacology and Therapeutics* 1989; **45:** 56.

Flumazenil used for antagonizing the central effects of midazolam and diazepam in outpatients. Jensen S, Knudsen L *et al. Acta Anaesthesiologica Scandinavica* 1989; **33:** 26.

Halothane suppresses slow inward currents in hippocampal slices. Krnjevic K, Puil E. *Canadian Journal of Physiology and Pharmacology* 1988; **66:** 1570.

Chronic diazepam treatment produces regionally specific changes in GABA-stimulated chloride influx. Marley RJ, Gallager DW. *European Journal of Pharmacology* 1989; **159:** 217.

The effect of anesthetics on lymphatic contractility. McHale NG, Thornbury KD. *Microvascular Research* 1989; **37:** 70.

Inhibition of halothane-induced lipid peroxidation by misoprostol without hepatoprotection. Siegers CP, Heger B *et al. Toxicology* 1988; **53:** 213.

Influence of anesthetics—nitrous oxide in particular—on electromyographic response evoked by transcranial electrical stimulation of the cortex. Zentner J, Kiss I, Ebner A. *Neurosurgery* 1989; **24:** 253.

### *Analgesic agents*

Induction of anesthesia with small doses of sufentanil or fentanyl: dose versus EEG response, speed of onset, and thiopental requirement. Bowdle TA, Ward RJ. *Anesthesiology* 1989; **70:** 26.

Transdermal fentanyl for postoperative pain management. Caplan RA, Ready LB *et al. Journal of the American Medical Association* 1989; **261:** 1036.

Sufentanil pharmacokinetics in patients with cirrhosis. Chauvin M, Ferrier C *et al. Anesthesia and Analgesia* 1989; **68:** 1.

Naloxone reversal of buprenorphine-induced respiratory depression. Gal TJ. *Clinical Pharmacology and Therapeutics* 1989; **45:** 66.

Effects of loperamide-oxide on fentanyl drug discrimination in rats. Meert TF, Niemegeers JE. *Drug Development Research* 1988; **15:** 415.

Chest wall rigidity during fentanyl and midazolam-fentanyl induction—ventilatory and haemodynamic effects. Neidhart P, Burgener MC *et al. Acta Anaesthesiologica Scandinavica* 1989; **33:** 1.

Naloxone enhances the response to hypercapnia of spinal and cranial respiratory nerves. Overholt JL, Mitra J *et al. Respiration Physiology* 1988; **74:** 299.

Cardiovascular and respiratory effects of intracerebroventricular administration of pentazocine in anesthetized rats. Safta L, Badau SD *et al. Current Therapeutic Research* 1989; **45:** 93.

Studies on morphine disposition—influence of general anaesthesia on plasma concentrations of morphine and its metabolites. Sear JW, Hand CW *et al. British Journal of Anaesthesia* 1989; **62:** 22.

Studies on morphine disposition—influence of renal failure on the kinetics of morphine and its metabolites. Sear JW, Hand CW *et al. British Journal of Anaesthesia* 1989; **62:** 28.

Opioids a better treatment for acute than tardive akathisia: possible role for the endogenous opiate system in neuroleptic-induced akathisia. Walters AS, Hening WA. *Medical Hypotheses* 1989; **28:** 1.

### *Muscle relaxants*

Combined H1 and H2 receptor blockade attenuates the

---

The collator of this section is Dr L. Kaufman, MD, FFARCS, 145 Harley Street, London W1N 2DE. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

cardiovascular effects of high dose atracurium in rabbits. HOSKING MP, LENNON RL, GRONERT GA. *Life Sciences* 1989; **44:** 347.

Intramuscular pressure and muscle blood flow in supraspinatus. JARVHOLM U, STYF J *et al. European Journal of Applied Physiology and Occupational Physiology* 1988; **58:** 219.

Inhibition of acetylcholinesterase by the H2-receptor antagonist nizatidine. KOUNENIS G, VOUTSAS D *et al. Journal of Pharmacobio-Dynamics* 1988; **11:** 767.

The effect of cholinesterase inhibitors on SFEMG in myasthenia gravis. MASSEY JM, SANDERS DB, HOWARD JF JR. *Muscle and Nerve* 1989; **12:** 154.

Ankle dorsiflexor twitch properties in malignant hyperthermia. QUINLAN JG, IAIZZO PA *et al. Muscle and Nerve* 1989; **12:** 119.

*Other drugs*

A molecular basis for bidirectional communication between the immune and neuroendocrine systems. BLALOCK JE. *Physiological Reviews* 1989; **69:** 1.

Interactions of monoamine oxidase with substrates and inhibitors. DOSTERT PL, BENEDETTI MS, TIPTON KF. *Medical Research Reviews* 1989; **9:** 45.

Minireview: thermodynamic analysis of the drug-receptor interaction. RAFFA RB, PORRECA F. *Life Sciences* 1989; **44:** 245.

Monoamine odase inhibitors revisited. WELLS DG, BJORKSTEN AR. *Canadian Journal of Anaesthesia* 1989; **36:** 64.

### Apparatus

Failure of electrocardiographic monitoring to detect cardiac arrest in patients with pacemakers. BROWNLEE JR, SERWER GA *et al. American Journal of Diseases of Children* 1989; **143:** 105.

Recovery room oxygenation: a comparison of nasal catheters and 40% oxygen masks. HUDES ET, MARANS HJ *et al. Canadian Journal of Anaesthesia* 1989; **36:** 20.

Practical use of duplex doppler analysis of the renal vasculature in critically ill patients. STEVENS PE, BOLSIN S *et al. Lancet* 1989; **1:** 240.

Pulse oximetry. TREMPER KK, BARKER SJ. *Anesthesiology* 1989; **70:** 98.

### Complications

Bronchopulmonary aspiration. LOCICERO J. *Surgical Clinics of North America* 1989; **69:** 71.

Complications of intravenous feeding catheters. MUGHAL MM. *British Journal of Surgery* 1989; **76:** 15.

### General anaesthetic procedures

Effects of tracheal extubation on coronary blood flow, myocardial metabolism and systemic haemodynamics. ELIA S, LIU P *et al. Canadian Journal of Anaesthesia* 1989; **36:** 2.

Prophylaxis against acid aspiration syndrome. Single oral dose of H2-antagonist on the evening before elevtive surgery. GALLAGHER EG, WHITE M *et al. Anaesthesia* 1988; **43:** 1011.

The future of general anaesthesia in the dental surgery: discussion paper. PADFIELD A. *Journal of the Royal Society of Medicine* 1989; **82:** 30.

Hypotensive anesthesia and blood loss. SOLLEVI A. *Acta Anaesthesiologica Scandinavica* 1988; **32** (Suppl. 89): 39.

### General interest

Lung function 8 years after neonatal ventilation. ANDREASSON B, LINDROTH M *et al. Archives of Disease in Childhood* 1989; **64:** 108.

Inadvertent diagnosis of pheochromocytoma after endoscopic premedication. BARANCIK M. *Digestive Diseases and Sciences* 1989; **34:** 136.

Monitoring the anaesthetist. LEADING ARTICLE. *Lancet* 1989; **1:** 251.

Effect of atrial natriuretic peptide on catecholamine release from human pheochromocytoma. NAKAMARU M, OGIHARA T *et al. Acta Endocrinologica* 1989; **120:** 107.

Tissue destruction by neutrophils. WEISS SJ. *New England Journal of Medicine* 1989; **320:** 365.

### Local analgesia

Intravenous prilocaine (citanest) for anesthesia in the lower extremity. AKTURK G, SOLAK M *et al. Israel Journal of Medical Sciences* 1989; **24:** 716.

Lidocaine pharmacokinetics during water immersion in normal humans. BLYDEN G, SILVERSTEIN F *et al. Journal of Applied Physiology* 1989; **66:** 57.

Regional anaesthesia and blood loss. MODIG J. *Acta Anaesthesiologica Scandinavica* 1989; **32** (Suppl. 89): 44.

### Spinal and epidural analgesia

Intrathecal opioids, potency and lipophilicity. MCQUAY HJ, SULLIVAN AF *et al. Pain* 1989; **36:** 111.

### Spinal opioids

Intrathecal bradykinin acts presynaptically on spinal noradrenergic terminals to produce antinociception in the rat. LANEUVILLE O, READER TA, COUTURE R. *European Journal of Pharmacology* 1989; **159:** 273.

Cardiovascular responses to intrathecal vasopressin in conscious and anesthesized rats. MARTINEZ-ARIZALA A, HOLADAY JW, LONG J. *American Journal of Physiology* 1989; **256** (No. 2 Part 2): R193.

### Obstetric anaesthesia and analgesia

Active and inactive renin throughout high risk pregnancy. AMBROSO GC, MORGANTI A *et al. Clinical and Experimental Hypertension* 1989; **7:** 75.

Pregnancy and travel. BARRY M, BIA F. *Journal of the American Medical Association* 1989; **261:** 728.

Sodium-renin-aldosterone relations in normal and hypertensive pregnancy. BROWN MA, NICHOLSON E, GALLERY EDM. *British Journal of Obstetrics and Gynaecology* 1989; **95:** 1237.

Pregnancy-induced hypertension; observations on chemical-physical properties of syncytiotrophoblast plasma membranes from human placenta. CESTER N, MAZZANTI L *et al. Clinical and Experimental Hypertension* 1988; **7:** 57.

Atrial natriuretic peptide and the renin angiotensin aldosterone system in normotensive and hypertensive pregnancy. DI LIETO A, CAMPANILE M *et al. Clinical and Experimental Hypertension* 1988; **7:** 89.

Epidural clonidine analgesia in obstetrics: sleep studies. EISEMACH JC, CASTRO MI *et al. Anesthesiology* 1989; **70:** 51.

Prevention of pre-eclampsia: pathophysiological rationale for the use of low-dose aspirin. GIANNATTASIO M, CORATELLI P *et al. Clinical and Experimental Hypertension* 1988; **7:** 149.

Plasma levels of atrial natriuretic peptides during pregnancy and post partum in the rat. JANSAKUL C, KING RG *et al. Journal of Endocrinology* 1989; **120:** 113.

Antihypertensive drug therapy during pregnancy. KAULHAUSEN H, WECHSLER E. *Clinical and Experimental Hypertension* 1988; **7:** 213.

The effect of sublingual nifedipine on uteroplacental blood flow in hypertensive pregnancy. LINDOW SW, DAVIES N *et al. British Journal of Obstetrics and Gynaecology* 1988; **95:** 1276.

Effect of cimetidine on maternal and fetal prolactin secretion during labor. MESSINIS IE, TSIRKAS N *et al. Journal of Endocrinological Investigation* 1988; **11:** 785.

Atrial natriuretic peptide (ANP) during pregnancy. NIESERT S, KAULHAUSEN H. *Clinical and Experimental Hypertension* 1988; **7:** 99.

Artial natriuretic factor as a marker of the intravascular volume conditions in normal and hypertensive pregnancies. STRATTA P, CANAVESE C *et al. Clinical and Experimental Hypertension* 1988; **7:** 107.

Should hyperbaric oxygen be used to treat the pregnant patient for acute carbon monoxide poisoning? VAN HOESEN KB, CAMPORESI EM *et al. Journal of the American Medical Association* 1989; **261:** 1039.

### Paediatric anaesthesia and intensive care

Morbidity for survivors of extracorporeal membrane oxygenation—neurodevelopmental outcome at 1 year of age. GLASS P, MILLER M, SHORT B. *Pediatrics* 1989; **83:** 72.

Acute effects of instillation of surfactant in severe respiratory distress syndrome. Halliday HL, McCord FB *et al. Archives of Disease in Childhood* 1989; **64** (special issue): 13.

Cerebral oxygenation and blood flow in infant and young adult rats. Kreisman NR, Olson JE *et al. American Journal of Physiology* 1989; **256** (No. 1 Part 2): R78.

Response of normal infants to inhaled histamine. Lesouef PN, Geelhoed GC *et al. American Review of Respiratory Disease* 1989; **139:** 62.

Lung aeration and lung water dynamics in artificially ventilated newborn lambs. Maloney JE, Kondo C *et al. Journal of Applied Physiology* 1989; **66:** 1.

Sleeping position and infant bedding may predispose to hyperthermia and the sudden infant death syndrome. Nelson EAS, Taylor BJ, Weatherall IL. *Lancet* 1989; **1:** 199.

Preductal and postductal transcutaneous oxygen tension measurements in premature newborns with hyaline membrane disease. Pearlman SA, Maisels J. *Pediatrics* 1989; **83:** 98.

Neurologic complications of captopril treatment of neonatal hypertension. Perlman JM, Volpe JJ. *Pediatrics* 1989; **83:** 47.

Noradrenaline and dopamine in fetal compartment in physiologic and hypertensive pregnancies. Serri FG, Mauri A *et al. Clinical and Experimental Hypertension* 1989; **7:** 67.

Routine endotracheal cultures for the prediction of sepsis in ventilated babies. Slagle TA, Bifano EM *et al. Archives of Disease in Childhood* 1989; **64:** (special issue): 34.

High-frequency oscillatory ventilation compared with conventional mechanical ventilation in the treatment of respiratory failure in preterm infants. The Hifi Study Group E. Sinnett. *New England Journal of Medicine* 1989; **320:** 88.

Renal functional impairment in preterm neonates related to intrauterine indomethacin exposure. Van Der Heijden AJ, Provoost AP *et al. Pediatric Research* 1988; **24:** 644.

Intervention after birth asphyxia. Whitelaw A. *Archives of Disease in Childhood* 1989; **64:** 66.

Expiratory airflow patterns and gas exchange in the newborn infant: results of model simulations. Zamel D, Revow M, England SJ. *Respiration Physiology* 1989; **75:** 19.

### Cardiovascular system

#### *Physiology*

Effects of atrial natriuretic peptide on systemic haemodynamics and cardiac function in normal man. Allen MJ, Gilmour SM *et al. Cardiovascular Research* 1989; **23:** 70.

Ambulatory sudden cardiac death: Mechanisms of production of fatal arrhythmia on the basis of data from 157 cases. Bayes De Luna A, Coumel P, Leclercq JF. *American Heart Journal* 1989; **117:** 151.

Relationship between phasic changes in human skin blood flow and autonomic tone. Bernardi L, Rossi M *et al. Microvascular Research* 1989; **37:** 16.

Gas exchange and metabolic transients in heart transplant recipients. Cerretelli P, Grassi B *et al. Respiration Physiology* 1988; **74:** 355.

Improved use of arterial blood gas analysis in suspected pulmonary embolism. Cvitanic O, Marino PL. *Chest* 1989; **95:** 48.

The role of adenosine and prostacyclin in coronary flow regulation in healthy man. Edlund A, Sollevi A, Wennmalm A. *Acta Physiologica Scandinavica* 1989; **135:** 39.

Classification of deaths after myocardial infarction as arrhythmic or nonarrhythmic (the cardiac arrhythmia pilot study). Greene HL, Richardson DW *et al. American Journal of Cardiology* 1989; **63:** 1.

Regional venous outflow, blood volume, and sympathetic nerve activity during severe hypoxia. Hoka S, Bosnjak ZJ *et al. American Journal of Physiology* 1989; **256** (No. 1 Part 2): H162.

Electrolyte disarray and cardiovascular disease. Hollifield JW. *American Journal of Cardiology* 1989; **63:** B21.

Delayed after depolarizations in heart muscle—mechanisms and relevance. 2. January CT, Fozzard HA. *Pharmacological Reviews* 1988; **40:** 219.

Risk factors in hypertension. Kannel WB *Journal of Cardiovascular Pharmacology* 1989; **13** (Suppl. 1): S4.

The myocardium in congestive heart failure. Katz AM. *American Journal of Cardiology* 1989; **63:** A12.

Reperfusion pulmonary edema. Klausner JM, Paterson IS *et al. Journal of the American Medical Association* 1989; **261:** 1030.

Hypoxic reperfusion attenuates postischemic microvascular injury. Korthuis RJ, Smith JK, Carden DL. *American Journal of Physiology* 1989; **256** (No. 1 Part 2): H315.

Contribution of neurogenic mechanisms to control of intrinsic heart rate. Machado BH, Brody MJ. *American Journal of Physiology* 1989; **256** (No. 1 Part 2): R231.

Noradrenaline attenuates the natriuretic effect of atrial natriuretic factor in man. McMurray JJ, Seidelin PH *et al. British Journal of Clinical Pharmacology* 1989; **27:** 7.

Clinical implications of the aging heart. Morley JE, Reese SS. *American Journal of Medicine* 1989; **86:** 77.

Atrial natriuretic peptide vascular receptor: regulation of low-affinity binding by calcium. Morton JJ, Beattie EC, Lyall F. *Clinical Science* 1989; **76:** 9.

Cardiovascular failure and apnea in shock. Nava S, Bellemare F. *Journal of Applied Physiology* 1989; **66:** 184.

Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography. I. Physiologic and pathophysiologic features. Nishimura RA, Housmans PR *et al. Mayo Clinic Proceedings* 1989; **64:** 71.

Renal actions of atrial natriuretic factor. Raine AEG, Firth JG, Ledingham JGG. *Clinical Science* 1989; **76:** 1.

Calcium mobilization and cardiac inotropic mechanisms. Reiter M. *Pharmacological Reviews* 1988; **40:** 189.

Peripheral circulation in septic shock. Thijs LG, Groeneveld ABJ. *Applied Cardiopulmonary Pathophysiology* 1988; **2:** 203.

Prevalence of nocturnal hypoxaemia amongst men with mild to moderate hypertension. Warley ARH, Mitchell JH, Stradling J. *Quarterly Journal of Medicine* 1988; **68:** 637.

ANP concentrations in hypoxic secondary pulmonary hypertension: relation to haemodynamic and blood gas variables and response to supplemental oxygen. Winter R, Davidson AC *et al. Thorax* 1989; **44:** 58.

Direct and neurohumoral cardiovascular effects of atrial natriuretic peptide. Woods RL, Oliver JR, Korner PI. *Journal of Cardiovascular Pharmacology* 1989; **13:** 177.

Erythropoietin. Zanjani ED, Ascensao JL. *Transfusion* 1989; **29:** 46.

#### *Treatment and medication*

Provocation of bradycardia and hypotension by isoproterenol and upright posture in patients with unexplained syncope. Almquist A, Goldenberg IF *et al. New England Journal of Medicine* 1989; **320:** 346.

Plasmin activity and complement activation during storage of citrated platelet concentrates. Bode AP, Miller DT *et al. Journal of Laboratory and Clinical Medicine* 1989; **113:** 88.

Pulmonary function and airway responsiveness during long-term therapy with captopril. Boulet LP, Milot J *et al. Journal of the American Medical Association* 1989; **261:** 413.

Renal and hormonal effects of phosphodiesterase-III inhibition in congestive heart failure. Cody RJ. *American Journal of Cardiology* 1989; **63:** A31.

Editorial—Perioperative red blood-cell transfusion. Cowell HR. *Journal of Bone and Joint Surgery* 1989; **71A:** 1.

Enzymatic estimation of the extent of irreversible myocardial injury early after reperfusion. Devries SR, Jaffe AS *et al. American Heart Journal* 1989; **117:** 31.

Elective deep hypothermia with total circulatory arrest—changes in plasma creatine kinase BB, blood glucose, and clinical variables. Ekroth R, Thompson RJ *et al. Journal of Thoracic and Cardiovascular Surgery* 1989; **97:** 30.

Pathophysiology of hypertension: effects of calcium antagonists on heart and kidney. Frohlich ED. *Journal of Cardiovascular Pharmacology* 1989; **13** (Suppl. 1): S11.

Cardiopulmonary toxicity of adoptive immunotherapy. Glauser FL, Deblois G *et al. American Journal of the Medical Sciences* 1988; **296:** 406.

Intraoperative autologous transfusion in orthopaedic patients. Goulet JA, Bray TJ *et al. Journal of Bone and Joint Surgery* 1989; **71A:** 3.

Review: treatment of pain in acute myocardial infarction. Herlitz J, Hjalmarson A, Waagstein F. *British Heart Journal* 1989; **61:** 9.

Review of long-term trials with nitrendipine. Hulthen UL, Katzman PL. *Journal of Cardiovascular Pharmacology* 1988; **12** (Suppl. 4): S11.

Drug management of the cardiac transplant patient. Hunt SA. *Cardiovascular Drugs and Therapy* 1988; **2:** 687.

The use of intravenous amiodarone in the acute therapy of life-threatening tachyarrhythmias. Kadish A, Morady F. *Progress in Cardiovascular Diseases* 1989; **31:** 281.

Plasma volume substitution. Karanko MS. *Acta Anaesthesiologica Scandinavica* 1988; **32** (Suppl. 89): 54.

ECG risk factors for sudden death. Kreger B. *Journal of Electrocardiology* 1988; **21** (Suppl. 1): S35.

Noninvasive predictors of sudden cardiac death in patients with coronary artery disease. Lampert S, Lown B *et al. Journal of Electrocardiology* 1988; **21** (Suppl.): S36.

The decision not to resuscitate: talking with patients and families. Latimer E. *Canadian Medical Association Journal* 1989; **140:** 133.

Negative pressure ventilation—effects on ventilation during sleep in normal subjects. Levy RD, Bradley TD *et al. Chest* 1989; **95:** 95.

Respiratory muscle performance in normal elderly subjects and patients with COPD. Morrison NJ, Richardson J *et al. Chest* 1989; **95:** 90.

Heme in the treatment of porphyrias and hematological disorders. Mustajoki P, Tenhunen R *et al. Seminars in Hematology* 1989; **26:** 1.

New transfusion practice and haemostasis. Myllyla G. *Acta Anaesthesiologica Scandinavica* 1988; **32** (Suppl. 89): 76.

Therapeutic options in the management of chronic heart failure—is there a drug of first choice? Packer M. *Circulation* 1989; **79:** 198.

Placebo-controlled, randomized trial of warfarin and aspirin for atrial fibrillation. Petersen P, Boysen G *et al. Lancet* 1989; **1:** 175.

Lack of effect of nicardipine and diltiazem on glucose—and arginine-induced insulin release in obese subjects. Pezzarossa A, Cimicchi M *et al. Cardiovascular Drugs and Therapy* 1988; **2:** 669.

Sleep quality and pulmonary function in the healthy elderly. Phillips B, Berry D *et al. Chest* 1989; **95:** 60.

Cardiovascular management in the capillary leak phase of early ARDS. Santman FW. *Applied Cardiopulmonary Pathophysiology* 1988; **2:** 225.

Sudden death and silent myocardial ischemia. Sheps DS, Heiss G. *American Heart Journal* 1989; **117:** 177.

Review: prostaglandin El and arterial occlusive disease: pharmacological considerations. Simmet TH, Peskar BA. *European Journal of Clinical Investigation* 1988; **18:** 549.

L-649, 923: An antagonist of cardiac and vascular leukotrinene D4 receptors. Siren AL, Eimerl J, Feuerstein G. *Journal of Cardiovascular Pharmacology* 1989; **13:** 210.

Simultaneous infusion of nitroglycerin and nitroprusside to offset adverse effects of vasopressin during portosystemic shunting. Sirinek KR, Adcock DK, Levine BA. *American Journal of Surgery* 1989; **157:** 33.

The noninvasive evaluation of syncope of suspected cardiovascular origin. Strasberg B, Sagie A *et al. American Heart Journal* 1989; **117:** 160.

Usefulness of isoproterenol during atrial fibrillation in evaluation of asymptomatic Wolff-Parkinson-White pattern. Szabo TS, Klein GJ *et al. American Journal of Cardiology* 1989; **63:** 187.

Should the elderly be resuscitated following out-of-hospital cardiac arrest? Tresch DD, Thakur RK *et al. American Journal of Medicine* 1989; **86:** 145.

Comparison of high-dose with low-dose subcutaneous heparin to prevent left ventricular mural thrombosis in patients with acute transmural anterior MI. Turpie AGG, Robinson JG *et al. New England Journal of Medicine* 1989; **320:** 352.

Crystalloid versus colloid fluid resuscitation—a meta-analysis of mortality. Velanovich V. *Surgery* 1989; **105:** 65.

Pathophysiological arguments for vasodilators in cardiac failure. Vogt A, Neuhaus KL, Kreuzer H. *Cardiovascular Drugs and Therapy* 1988; **2:** 647.

Myocardial salvage after regional beta-adrenergic blockade. Wappel M, Zalewski A *et al. American Heart Journal* 1989; **117:** 37.

Intra-operative autologous transfusion in revision total hip arthroplasty. Wilson WJ. *Journal of Bone and Joint Surgery* 1989; **71A:** 8.

Hemodynamic effects of nifedipine and oxygen in children with pulmonary hypertension. Wimmer M, Schlemmer M, Ebner F. *Cardiovascular Drugs and Therapy* 1988; **2:** 661.

## Respiration

### *Physiology*

Chest wall impedance partitioned into rib cage and diaphragm-abdominal pathways. Barnas GM, Yoshino K *et al. Journal of Applied Physiology* 1989; **66:** 350.

Respiratory functions of the larynx. Bartlett D Jr. *Physiological Reviews* 1989; **69:** 33.

A dynamic analysis of the ventilatory response to hypoxia in man. Bertholon JF, Eugene M *et al. Journal of Physiology* 1989; **408:** 473.

Alveolar hypoxia, inhibition of hypoxic pulmonary vasoconstriction, and permeability edema. Cheney FW, Eisenstein BL, Bishop MJ. *Respiration Physiology* 1989; **75:** 11.

Influence of airway calibre on the intrapulmonary dose and distribution of inhaled aerosol in normal and asthmatic subjects. Chung KF, Jeyasingh K, Snashall PD. *European Respiratory Journal* 1988; **1:** 890.

Abdominal muscle use during breathing in unanesthetized dogs. De Troyer A, Gilmartin JJ, Ninane V. *Journal of Applied Physiology* 1989; **66:** 20.

Role of absorptive and secretory processes in hydration of the airway surface. Frizzell RA. *American Review of Respiratory Disease* 1988; **138** (Suppl.): S3.

Magnetic resonance imaging of the thorax. Gamsu G, Sostman D. *American Review of Respiratory Disease* 1989; **139:** 254.

Neuroendocrine dysfunction in sleep apnea: reversal by continuous positive airways pressure therapy. Grunstein RR, Handelsman DJ *et al. Journal of Clinical Endocrinology and Metabolism* 1989; **68:** 352.

The mechanics of airway narrowing in asthma. James AL, Pare PD, Hogg JC. *American Review of Respiratory Disease* 1989; **139:** 242.

Diltiazem, verapamil, and nifedipine inhibit theophylline-enhanced diaphragmatic contractility. Kolbeck RC, Speir WA. *American Review of Respiratory Disease* 1989; **139:** 139.

Abnormal breathing during sleep and chemical control of breathing during wakefulness in patients with sleep apnea syndrome. Kunitomo F, Kimura H *et al. American Review of Respiratory Disease* 1989; **139:** 164.

Magnesium and the lungs. Mathew R, Altura BM. *Magnesium* 1988; **7:** 173.

Characterization of adenosine receptors in human pulmonary arteries. McCormack DG, Clarke B, Barnes PJ. *American Journal of Physiology* 1989; **256** (No. 1 Part 2): H41.

Maximal static respiratory pressures in the normal elderly. McElvaney G, Blackie S *et al. American Review of Respiratory Disease* 1989; **139:** 227.

Mechanism of ribe cage inspiratory muscle recruitment in diaphragmatic paralysis. Ninane V, Farkas GA *et al. American Review of Respiratory Disease* 1989; **139:** 146.

Mouth pressure curve on abrupt interruption of airflow during forced expiration. Ohya N, Huang J *et al. Journal of Applied Physiology* 1989; **66:** 509.

Acute post-traumatic respiratory physiology and insufficiency. Pepe PE. *Surgical Clinics of North America* 1989; **69:** 157.

Sleep apnoea. Prowse K, Allen MB. *British Journal of Diseases of the Chest* 1988; **82:** 329.

Does acute hypoxemia blunt sympathetic activity in hyperthermia? Rowell LB, Brengelmann GL *et al. Journal of Applied Physiology* 1989; **66:** 28.

Calibration of respiratory inductive plethysmograph during natural breathing. Sackner MA, Watson H *et al. Journal of Applied Physiology* 1989; **66:** 410.

Increased plasma oncotic pressure inhibits pulmonary fluid transport when pulmonary pressures are elevated. Wareing TH, Gruber MA *et al. Journal of Surgical Research* 1989; **46:** 29.

Severe hypoxia: lessons from high altitude. West JB. *Applied Cardiopulmonary Pathophysiology* 1988; **2:** 247.

Rate of ventilatory acclimatization to extreme altitude. West JB. *Respiration Physiology* 1988; **74:** 323.

Expiratory mechanics before and after uncomplicated heart surgery. Zin WA, Caldeira MPR *et al. Chest* 1989; **95:** 21.

*Treatment and medication*

The inverted ratio ventilation and the use of PEEP in asthma. Anderson JB. *Applied Cardiopulmonary Pathophysiology* 1988; **2:** 255.

Dopamine effects on diaphragmatic strength during acute respiratory failure in chronic obstructive pulmonary disease. Aubier M, Murciano D *et al. Annals of Internal Medicine* 1989; **110:** 17.

Management of patients with glottic and subglottic stenosis resulting from thermal burns. Flexon PB, Cheney ML *et al. Annals of Otology, Rhinology and Laryngology* 1989; **98:** (No. 1 Part 1): 27.

Modification of the oxygen affinity and intracellular hemoglobin concentration of normal and sickle cells by means of an osmotic pulse. Franco RS, Barker RL. *Journal of Laboratory and Clinical Medicine* 1989; **113:** 58.

Nocturnal asthma: snoring, small pharynx and nasal CPAP. Guilleminault C, Quera-Salva MA *et al. European Respiratory Journal* 1988; **1:** 902.

Lung function and exercise performance in hyperthyroidism before and after treatment. Kendrick AH, Oreilly JF, Laszio G. *Quarterly Journal of Medicine* 1988; **68:** 615.

Ozone-induced changes in pulmonary function and bronchial responsiveness in asthmatics. Kreit JW, Gross KB *et al. Journal of Applied Physiology* 1989; **66:** 217.

Effects of oral morphine on breathlessness and exercise tolerance in patients with chronic obstructive pulmonary disease. Light RW, Muro JR *et al. American Review of Respiratory Disease* 1989; **139:** 126.

Status asthmaticus and mechanical ventilation. Perret C. *Applied Cardiopulmonary Pathophysiology* 1988; **2:** 241.

Gangrene of the lung. Phillips LG, Rao KVS. *Journal of Thoracic and Cardiovascular Surgery* 1989; **97:** 114.

Diagnostic criteria for adult respiratory distress syndrome: time for reappraisal. Rocker GM, Wiseman MS *et al. Lancet* 1989; **1:** 120.

Naloxone does not alter response to hypercapnia or resistive loading in chronic obstructive pulmonary disease. Simon PM, Pope A *et al. American Review of Respiratory Disease* 1989; **139:** 134.

Disappointment and promise in the pharmacologic treatment of obstructive sleep apnea. Strohl KP. *Journal of Laboratory and Clinical Medicine* 1989; **113:** 6.

## Central nervous system

*Physiology*

Cerebral autoregulation dynamics in humans. Aaslid R, Lindegaard KF *et al. Stroke* 1989; **20:** 45.

Orthostatic hypotension as a risk factor for symptomatic occlusive cerebrovascular disease. Dobkin BH. Neurology 1989; **39:** 30.

Hypoxic neuropathy—does hypoxia play a role in diabetic neuropathy?—The 1988 Robert Wartenberg Lecture. Dyck PJ. *Neurology* 1989; **39:** 111.

ATP and brain function. Erecinska M, Silver IA. *Journal of Cerebral Blood and Metabolism* 1989; **9:** 2.

Effects of hypovolemic hypotensive shock on somatosensory and motor evoked potentials. Haghighi SS, Oro JJ. *Neurosurgery* 1989; **24:** 246.

Brain hypoxia preferentially stimulates genioglossal EMG responses to $CO_2$. Hutt DA, Parisi RA *et al. Journal of Applied Physiology* 1989; **66:** 51.

Monoamine oxidases of the human brain and liver. Kalaria RN, Mitchell MJ, Harik SI. *Brain* 1988; **111** (Part 6): 1441.

Validity of cerebral arterial blood flow calculations from velocity measurements. Kontos HA. *Stroke* 1989; **20:** 1.

CSF acetylcholinesterase levels are reduced in multiple system atrophy with autonomic failure. Polinsky RJ, Holmes KV *et al. Neurology* 1989; **39:** 40.

Cerebral arteriovenous oxygen difference as an estimate of cerebral blood flow in comatose patients. Robertson CS, Narayan RK *et al. Journal of Neurosurgery* 1989; **70:** 222.

Influence of lung volume in sleep apnoea. Series F, Cormier Y *et al. Thorax* 1989; **44:** 52.

*Treatment and medication*

Tyramine conjugation test for prediction of treatment response in depressed patients. Hale AS, Sandler M *et al. Lancet* 1989; **1:** 234.

Cerebral blood flow and metabolism during adenosine-induced hypotension in patients undergoing cerebral aneurysm surgery. Lagerkranser M, Bergstrand G *et al. Acta Anaesthesiologica Scandinavica* 1989; **33:** 15.

Administration of intravenous urea and normal saline for the treatment of hyponatremia in neurosurgical patients. Reeder RF, Harbaugh RE. *Journal of Neurosurgery* 1989; **70:** 201.

Role of dopamine receptors in neurological drug treatment. Rinne UK. *Annals of Clinical Research* 1988; **20:** 334.

The doppler $CO_2$ test to exclude patients not in need of extracranial intracranial bypass surgery. Widder B. *Journal of Neurology, Neurosurgery and Psychiatry* 1989; **52:** 38.

Traumatic shock and head injury: effects of fluid resuscitation on the brain. Wisner D, Busche F *et al. Journal of Surgical Research* 1989; **46:** 49.

## Endocrine and metabolic

*Physiology*

Clinical aspects of sucrose and fructose metabolism. Bantle JP. *Diabetes Care* 1989; **12:** 56.

Chemistry of buffer equilibria in blood plasma. Boron WF. In: Seldin DW, Giebisch G, eds. *Regulation of acid-base balance*. New York: Raven Press 1989: 3.

Progression of renal insufficiency—role of blood pressure. Brazy PC, Stead WW, Fitzwilliam JF. *Kidney International* 1989; **35:** 670.

Clinical pathophysiology and metabolic effects of hypothyroidism. Burgi U, Konig MP. *Bailliere's Clinical Endocrinology and Metabolism* 1988; **2:** 567.

Fatigue and cardiac and endocrine metabolic response to exercise after abdominal surgery. Christensen T, Stage JG *et al. Surgery* 1989; **105:** 46.

Diagnosis of adrenal insufficiency. Clayton RN. *British Medical Journal* 1989; **298:** 271.

New concepts in renal ammonium excretion. Good DW In: Seldin DW, Giebisch G, eds. *Regulation of acid-base balance*. New York: Raven Press 1989: 169.

Biosynthesis and secretion of insulin. Howell SL, Birg G ST J. *British Medical Bulletin* 1989; **45:** 19.

Muscle function in patients with primary hyperparathyroidism. Joborn C, Rastad J *et al. Muscle and Nerve* 1989; **12:** 87.

Intra-operative measurement of adrenocorticotropic hormone in peripituitary blood in Cushing's disease. Ludecke DK. *Neurosurgery* 1989; **24:** 201.

Muscle glycogen availability and temperature regulation in humans. Martineau L, Jacobs I. *Journal of Applied Physiology* 1989; **66:** 72.

The metabolism and metabolic effects of ketoacids. May RC, Mitch WE. *Diabetes/Metabolism Reviews* 1989; **5:** 71.

Minireview: Melatonin: perspectives in the Life Sciences. Miles A. *Life Sciences* 1989; **44:** 375.

Characterization of insulin resistance after surgery. Nordenstrom J, Sonnenfeld T, Arner P. *Surgery* 1989; **105:** 28.

Increased serum cortisol binding in chronic active hepatitis. Orbach O, Schussler GC. *American Journal of Medicine* 1989; **86:** 39.

Pharmacokinetics and metabolism of neurotensin in man. Pedersen JH, Andersen HO *et al. Journal of Clinical Endocrinology and Metabolism* 1989; **68:** 294.

Overall acid-base regulation by the kidney. Sabatini S, Kurtzman NA. In: Seldin DW, Giebisch G, eds. *Regulation of acid-base balance*. New York: Raven Press 1989; 185.

Basis for myocardial mechanical defects associated with non-insulin-dependent diabetes. Schaffer SW, Mozaffari MS *et al. American Journal of Physiology* 1989; **256** (No. 1 Part 1): E25.

Naloxone affects the release of cortisol, but not of vasopressin or oxytocin in dehydrated sheep. Thornton SN, Parrott RF. *Acta Endocrinologica* 1989; **120:** 50.

Adrenergic modulation of adrenocorticotropin responses to insulin-induced hypoglycemia and corticotropin-releasing hormone. Tomori N, Suda T *et al. Journal of Clinical Endocrinology and Metabolism* 1989; **68:** 87.

Plasma arginine vasopressin levels and arterial pressure during open heart surgery. Woods WGA, Forsling ML, Lequesne LP. *British Journal of Surgery* 1989; **76:** 29.

*Treatment and medication*

Diabetic emergencies. Alberti KGMM. *British Medical Bulletin* 1989; **45:** 242.

Diuretics—a risk in the long-term treatment of hypertensive patients. Amery A *et al. Journal of Hypertension* 1988; **6:** 925.

Clinical syndromes of respiratory acidosis alkalosis. Elliott CG, Morris AH. In: Seldin DW, Giebisch G, eds. *Regulation of acid-base balance*. New York: Raven Press; 1989; 483.

Mechanism of the antiproteinuric effect of indomethacin in nephrotic humans. Golbetz H, Black V *et al. American Journal of Physiology* 1989; **256** (No. 1 Part 2)**:** F44.

Diuretic effect of nitrendipine contributes to its antihypertensive efficacy: a review. Kazda S, Hirth C, Stasch JP. *Journal of Cardiovascular Pharmacology* 1988; **12** (Suppl. 4)**:** S1.

Severe hypoglycemia as a short-term side-effect of the somatostatin analog SMS 201–995 in insulin-dependent diabetes mellitus. Navascues I, Gil J et al. Hormone and Metabolic Research 1988; **20:** 749.

Effect of nicardipine on insulin secretion, glucose and lipid metabolism in hypertensive, non-insulin dependent diabetics. Pasanisi F, Vaccaro O *et al. European Journal of Clinical Pharmacology* 1989; **36:** 1.

Glucose and insulin metabolism in cirrhosis. Petrides AS, Defronzo RA. *Journal of Hepatology* 1989; **8:** 107.

Bilateral massive adrenal hemorrhage: early recognition and treatment. Rao RH, Vagnucci AH, Amico JA. *Annals of Internal Medicine* 1989; **110:** 227.

## Pain

*Treatment and medication*

Comparison of ketamine and pethidine in experimental and postoperative pain. Maurset A, Skoglund LA *et al. Pain* 1989; **36:** 37.

The efficacy of benorylate in postoperative dental pain. Moore U, Seymour RA *et al. European Journal of Clinical Pharmacology* 1989; **36:** 35.

Spinal cord stimulation for relief of chronic pain in vasospastic disorders of the upper limbs. Robaina FJ, Dominguez M *et al. Neurosurgery* 1989; **24:** 63.

Analgesia produced by normal doses of opioid antagonists alone and in combination with morphine. Vaccarino AL, Tasker RAR, Melzack R. *Pain* 1989; **36:** 103.

# Canadian Journal of Anaesthesia

**Editor-in-Chief**
David R. Bevan
*Montreal, Quebec*

**Editor Emeritus**
R.A. Gordon
*Toronto, Ontario*

**Editorial Board**
Alan D. Baxter
*Ottawa, Ontario*

Thomas J. Coonan
*Halifax, Nova Scotia*

François Donati
*Montreal, Quebec*

A.O. Davies
*North Bay, Ontario*

Peter G. Duncan
*Saskatoon, Saskatchewan*

Jean-François Hardy
*Montreal, Quebec*

Richard Knill
*London, Ontario*

Geoffrey L. Dunn
*Hamilton, Ontario*

R. Kozody
*Edmonton, Alberta*

René Martin
*Sherbrooke, Quebec*

Brian Milne
*Kingston, Ontario*

William H. Noble
*Toronto, Ontario*

Richard J. Palahniuk
*Winnipeg, Manitoba*

David John Stewart
*Vancouver, British Columbia*

Leo Strunin
*Calgary, Alberta*

The Canadian Journal of Anaesthesia is a highly regarded international publication now in its 36th year. Formerly the Canadian Anaesthetists' Society Journal (Volumes 1-33, 1954-1986) the journal acquired both a new name and format in 1987.

Regular features include reports of investigations, informative review articles, clinical and technical reports, editorials, book reviews, correspondence, classified ads and meeting notices.

The Canadian Anaesthetists' Society continues to publish the Canadian Journal of Anaesthesia which appears bimonthly and includes the Annual Meeting Supplement with the regular May issue. This supplement contains refresher course outlines and abstracts of papers presented at the Society's Annual Meeting.

International in content and readership, consider the Canadian Journal of Anaesthesia for authoritative, up to date information on anaesthesia and related medicine.

## 1989 Subscription Information

Volume 36 (6 issues plus Annual Meeting Supplement) 1989
Individuals: $80.00 / Institutions: $115.00 / Air Mail: $60.00

All subscriptions begin with first issue of the calendar year.

Cheques should be made payable to the Canadian Journal of Anaesthesia and must be drawn on a Canadian or US bank account. The prices quoted are in Canadian dollars. VISA, Mastercard and American Express are accepted, please include expiry date.

ISSN: 0832–610X
Sample copies are available.

## Abstracted or indexed in:

Excerpta Medica, TSD Index Medicus; and available on microfilm through University Microfilms.

Please send cheques or information requests to:
**Canadian Journal of Anaesthesia**
**187 Gerrard Street East**
**Toronto, Ontario, Canada M5A 2E5**

Telephone: **(416) 923-1449**

# Contents: Anaesthesia, vol. 44, no. 6, June 1989

EDITORIAL

Sir Geoffrey Stephen William Organe, MA, MRCS, LRCP, MB, BChir, MD, FFARCS, FFRACS (Hon), FRCS, FFARCS (Hon), DA—25 December 1908–7 January 1989
*W.K. Pallister* 461

ORIGINAL ARTICLES

Crystalloid versus colloid for circulatory preload for epidural Caesarean section
*A.M. Murray, M. Morgan and J.G. Whitwam* 463

Alkalinisation of bupivacaine for sciatic nerve blockade
*D.M. Coventry and J.G. Todd* 467

Comparison of hyperbaric and plain bupivacaine with hyperbaric cinchocaine as spinal anaesthetic agents
*F.L. Roberts, E.C. Brown, R. Davis and M.J. Cousins* 471

Changes in cardiac output during epidural anaesthesia for Caesarean section
*S. Robson, S. Hunter, R. Boys, W. Dunlop and M. Bryson* 475

Inheritance of low plasma cholinesterase activity in two families with a history of suxamethonium sensitivity
*M. Whittaker, M. Berry and J.J. Britten* 480

CASE REPORTS

'Locked-in' syndrome. Occurrence after coronary artery bypass graft surgery
*D.J. Kenny and D.A.Luke* 483

Atracurium overdose in a small infant
*A.J. Charlton, N.J.N. Harper, D. Edwards and A.C. Wilson* 485

Paraplegia after coeliac plexus block
*M.J. Woodham and M.H. Hanna* 487

The management of Caesarean section in a patient with an intracranial arteriovenous malformation
*J.A. Laidler, I.J. Jackson and N. Redfern* 490

Failure of repeated blood patch in the treatment of spinal headache
*R.A. Fry and A. Perera* 492

APPARATUS

A new dual function nerve stimulator
*A.J. Sansome and J.G. de Courcy* 494

The Malawi anaesthetic machine. Experience with a new type of anaesthetic apparatus for developing countries
*P.M. Fenton* 498

FORUM

Serious morbidity attributable to anaesthesia. Considerations for prevention
*T. Pedersen and S.H. Johansen* 504

Hypoxaemia during outpatient dental anaesthesia
*N.A. Allen, D.J. Rowbotham and W.S. Nimmo* 509

Occupational exposure to nitrous oxide in four hospitals
*W.M Gray* 511

CORRESPONDENCE 515

BOOK REVIEWS 537

ANAESTHETIC LITERATURE 539

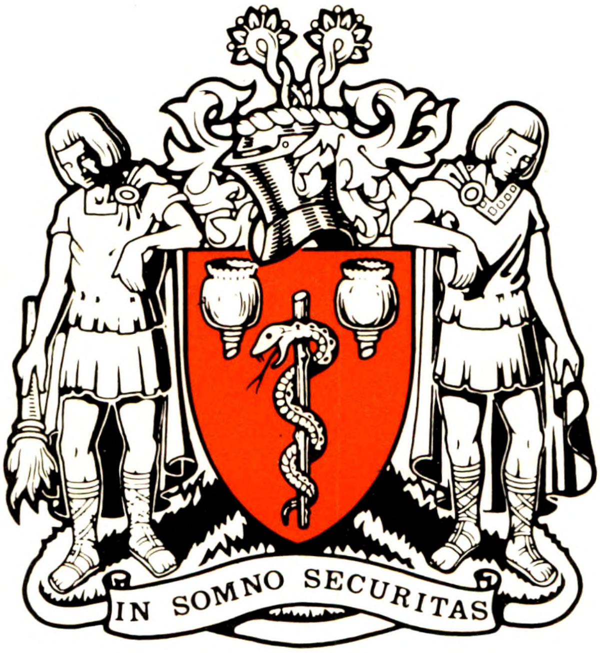
---

Typeset in Great Britain by Richard Clay Ltd, Bungay, Suffolk
Printed by The Whitefriars Press Ltd, member of BPCC Ltd, Tonbridge, Kent

# Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Volume 44 Number 7 July 1989



The Association of Anaesthetists of Great Britain and Ireland
*Patron*: HRH The Princess Margaret, Countess of Snowdon

Published for the Association by
Academic Press Grune & Stratton
London San Diego New York Boston
Sydney Tokyo Toronto

ISSN 0003-2409

*Some larger species of whale are able to remain submerged for up to an hour before surfacing to breathe. The picture shows a humpback whale (Megaptera novaeangliae).*

At each stage of the operative procedure, 'Diprivan' brings benefits to those concerned.

The anaesthetist achieves smooth induction and well controlled maintenance by repeat bolus or continuous infusion.

Early post-operative assessment by both the surgeon and the anaesthetist is possible, thanks to the patient's rapid recovery.

Above all, the patient quickly regains full mental clarity, usually free from unpleasant after effects, making the task of patient reassurance easier for the nursing staff.

For procedures expected to last up to one hour, 'Diprivan' has made total intravenous anaesthesia a reality.

---

**'DIPRIVAN' ▼ PRESCRIBING NOTES Use** Induction and maintenance of general anaesthesia for surgical procedures lasting up to one hour. **Presentation** Ready to use, isotonic, aqueous emulsion containing 10mg/ml propofol in a vehicle containing soybean oil and purified egg phosphatide. **Dosage and administration Induction** Titrate against response using approximately 4ml every 10 seconds in healthy adults and 2ml every 10 seconds in patients of ASA grades 3 and 4. Patients under 55 years are likely to require 2.0 to 2.5mg/kg, older patients may require approximately 20% less. **Maintenance** Usually 0.1 to 0.2mg/kg/min (6 to 12mg/kg/hr). Continuous infusion may require slightly higher rates for 10 to 20 minutes after induction. Alternatively repeat bolus injections of 25 to 50mg (2.5 to 5.0ml) may be used. **Paediatric Use** No experience in children or in mothers who are breast feeding. **Precautions** Do not mix prior to administration with other agents or infusion fluids. Hypotension and transient apnoea may occur during induction. Occasionally, hypotension may require use of i.v. fluids and lower rate of administration during maintenance. Apply caution in cardiac, respiratory, renal or hepatic impairment; in hypovolaemic or debilitated patients; and in disorders of fat metabolism or conditions where lipid emulsions should be used cautiously. On general principles, do not use in pregnancy except for termination. **Side effects** Bradycardia responsive to atropine has been reported. Epileptiform movements have occurred rarely in temporal relationship to 'Diprivan' but no causal relationship has been established. Nausea, vomiting and headache in a small proportion of patients. Very rarely, a clinical syndrome, which may include bronchospasm and erythema accompanied by hypotension, has been reported with 'Diprivan'. Pain on injection in a proportion of patients. Venous sequelae are rare. Minimal evidence of excitation on induction. **Product licence number** 29/0190 **Basic NHS cost** £3.98 per 20ml ampoule. 'Diprivan' is a trademark. Lower price available for hospitals. Further information is available from: ICI Pharmaceuticals (UK), Southbank, Alderley Park, Macclesfield, Cheshire. SK10 4TF

ICI
World Class

**Diprivan**
propofol

VERSATILE MAINTENANCE OF ANAESTHESIA

# Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

---

Editor J. N. LUNN
Associate Editor M. MORGAN
Assistant Editors R. GREENBAUM, A. R. AITKENHEAD, D. E. F. NEWTON
Editor of *Anaesthesia News* J. N. HORTON
*Editorial Board*
Chairman The President of the Association M. M. BURROWS
Members C. F. SCURR, P. J. F. BASKETT, J. EDMONDS-SEAL and a representative of the Junior Anaesthetists' Group
*Ex officio*
The Honorary Treasurer of the Association W. R. MACRAE
The Honorary Secretary of the Association W. L. M. BAIRD
The Immediate Past Honorary Secretary of the Association P. MORRIS

---

*Sub-editors of special sections*
L. KAUFMAN Anaesthetic literature
J. R. DAVIES Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

---

*Address for literary contributions* Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethics committee. A written statement of this acceptance may be requested by the Editor.

---

ANAESTHESIA: ISSN 0003-2409. Volume 44 1989, published monthly by Academic Press at 24–28 Oval Road, London NW1 7DX, UK, for the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
**All advertising** enquiries should be addressed to the Advertising Department, Anaesthesia, Harcourt Brace Jovanovich, 2nd Floor, 24–28 Oval Road, London NW1 7DX (Tel: 01-267 4466; Telex: 25775 ACPRES G; Fax: 01-482 2293).
Annual subscription price including postage: £108 UK and US $228 overseas. Subscription orders should be sent to Academic Press Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01-300 3322). Send notices of changes of address to the publisher at least 6–8 weeks in advance, including both old and new address.
Second class postage rate paid at Jamaica, NY 11431, USA.
Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Avenue, Elmomont, NY 11003, USA.
USA POSTMASTERS: send change of addresses to ANAESTHESIA, c/o Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, USA.
Printed in UK.
© 1989 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the USA. This consent is given on the condition, within the USA, that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, USA for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the USA.

**The 9000 Syringe Pump from Ohmeda. Designed to complement today's anaesthesia workstation.**

# Take your best shot.

Infusion anaesthesia. It's the ideal addition to your anaesthesia delivery capability.

To take advantage of all that IV anaesthesia techniques offer, an infusion pump adapted from critical care isn't enough.

You need the 9000 Syringe Pump. The one *for* anaesthesia.

The 9000 is designed and built by Ohmeda, the leader in anaesthesia systems, to meet your needs for more flexible, more controllable IV delivery at your workstation.

The 9000 was also developed in cooperation with major pharmaceutical manufacturers to complement the full range of shorter-acting, more controllable anaesthesia drugs–hypnotics, muscle relaxants, analgesics, hypotensives and inotropes.

**A smoother course in each case.**

With the 9000 Syringe Pump, the **full dose** can be delivered, including loading and maintenance doses, and intraoperative boli. No need for special set ups, added costs.

**During loading,** the 9000 administers the drug dose smoothly and evenly which can lessen the haemodynamic depressant effects of some drugs.

**During maintenance,** 0.1 mL/hr to 200 mL/hr output offers a flexible infusion range to manage the wide choice of regimes encountered in anaesthesia. A choice of standard syringes helps match size to dose to cut drug waste.

**Anytime,** selectable bolus delivery helps you quickly react to changing anaesthesia requirements such as increasing anaesthetic depth or muscle relaxation. No need for a second syringe. No need to remove a syringe from the pump.

**In the continuous infusion mode, the display indicates syringe size, volume infused and delivery rate.**

**If a bolus is selected, the display indicates the rate and the volume delivered in that bolus. When complete, the readout reverts to the continuous infusion display.**

The Ohmeda 9000. Not merely an infusion pump–today's advanced infusion anaesthesia *system* for the operating theatre.

Contact your Ohmeda representative or call 0279 442001 to make a 9000 Syringe Pump part of your system.

*Anaesthesia*, 1989, Volume 44, pages 545–546

# Editorial

## Neurophysiological monitoring

Neurophysiological monitoring in the operating theatre and in the intensive care unit is becoming increasingly important as attention is turned to safety, quality of care and audit of clinical practice. Historically, anaesthetists, with their special expertise in the pharmacological manipulation of consciousness and of the neuromuscular junction, have always practised applied neurophysiology. More recently, fundamental contributions into the scientific basis of anaesthesia and into methods to protect the brain from ischaemic damage have been made by anaesthetists using sophisticated electroencephalographic (EEG) and evoked potential monitoring techniques. Cognisant that the electrical activity of the mammalian brain may be reversibly depressed by narcosis and by ischaemia, clinical neurophysiologists have worked with surgical teams to depict depth of anaesthesia and to provide monitoring of the state of the brain and spinal cord during high risk procedures. Anecdotal accounts, and some more objective studies, suggest that many such procedures reduce morbidity and they may certainly help audit quality of work; however, few centres can mount comprehensive monitoring services for all risky procedures or even ensure that every patient is adequately and safely anaesthetised. It may be argued that there is a more realistic place for neurophysiological monitoring in the training of surgeons and anaesthetists. For example, a neurosurgical trainee can learn by auditory feedback from electrical potentials from the VIIIth cranial nerve when undue traction is putting the neuronal pathway at risk. He will not need the assistance of such monitoring throughout his professional life once he has learned to gauge the range of 'safe' retraction. Similarly, a trainee anaesthetist may learn by EEG feedback to give a smooth anaesthetic, without periods of excessive 'lightness' or depth. This lesson will provide a foundation for future practice, only requiring reinforcement when new agents are encountered. This application of neurophysiological monitoring as a component of training protocols is perhaps a more realistic aim than attempts to monitor everything.

However, nowadays clinical neurophysiologists and their technicians are regularly asked to provide extensive EEG and evoked potential monitoring services during spinal, neurosurgical, cardiac or vascular operations. They are also asked to help assess the effects of new anaesthetic agents and to monitor elective treatment of patients undergoing intensive care of major brain injuries. In a survey of members of the Association of British Clinical Neurophysiologists (1987), to which three quarters of the practising members responded, over 80% were found to be actively engaged in such activities in collaboration with their anaesthetic or surgical colleagues. Indeed several reported that surgeons were reluctant to undertake certain procedures without the precaution of either EEG or evoked potential monitoring even though, for some examples, no precise cost-benefit analysis was made. There seems little doubt that medicolegal considerations will increase the demands for these techniques as a routine; but until a technique has been shown to have a clear benefit for the patient such pressures may have to be resisted.

This relatively new area of collaborative work is undertaken with enthusiasm by most clinical neurophysiologists although, in our relatively small specialty, few are yet able to give sufficient time for a proper commitment. Most are concerned by the shortage of appropriate training and equipment as well as the inadequate staffing levels available for undertaking such tasks, both at technical and clinical levels.

It is timely as the provision of health care is reassessed in several countries, to consider who should undertake this type of work and what resources and training for neurophysiological monitoring should be made available. Most people would agree that these techniques require a team approach; the skills of appropriately trained clinical neurophysiologists and physiological measurement technicians complement those of the clinical teams in the operating theatre or intensive care unit. Neither the neurophysiologists nor the clinicians can provide an optimal monitoring service for the patient on their own. Close interaction is needed to define the risks that justify monitoring, to detail the precise aims, the required methodology and warning protocols and, importantly, to set realistic cost-benefit levels. Many of the procedures that will be used are relatively novel and may require technical research and development of novel combinations of established or newly devised techniques.

The implications of this development are that much cross-fertilisation is required on how best to find solutions for specific monitoring problems. Expertise can be shared and training in special techniques gained by means of individual apprenticeships, workshops and by publication of manuals of techniques and of National and International codes of practice. Intensive training courses and workshops are in fact already promoted and these draw upon the expertise of personnel from several disciplines who have experience in clinical monitoring involving neurophysiological methods. There are now several reports on the wide range of applications for EEG and evoked potential monitoring during surgery or intensive care with standards for methodology and recommendations about appropriate training and personnel.[1–11] The question of provision of funding for manpower and equipment has, as yet, received less attention. However, the newer information technologies and knowledge-based systems suggest that common databases and expertise eventually may be built into reasonably priced yet sophisticated equipment together with some form of teaching programmes, much as has been done for electromyography.[12–14] This will enable more uniform standards and provide a basis for audit of work.

The future holds considerable promise for better clinical practice as increasing expertise and more adequate staffing enable teams of surgeons, anaesthetists and clinical neurophysiologists to collaborate in using

0003-2409/89/070545+02

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

modern EEG, evoked potential and EMG techniques for training and usefully to monitor the wellbeing of their patients during high-risk procedures.

*Department of Neurological Sciences,*
*St Bartholomew's Hospital,*
*London EC1A 7BE*

P.F. Prior

## References

1. Levy WJ, Grundy B, Smith NT. Monitoring the electroencephalogram and evoked potentials during anesthesia. In: Saidman LJ, Smith NT, eds. *Monitoring in anesthesia,* 2nd edn. Boston: Butterworth, 1984: 228–67.
2. Shapiro HM. Anesthesia effects upon cerebral blood flow, cerebral metabolism, electroencephalogram, and evoked potentials. In: Miller RD, ed. *Anesthesia Vol. 2.* New York: Churchill-Livingstone, 1985: 1249–80.
3. Willatts SM, Walters FJ. *Anaesthesia and intensive care for the neurosurgical patient.* Oxford: Blackwell Scientific, 1986.
4. Pichlmayr I, Lips U, Künkel H. *The electroencephalogram in anesthesia. Fundamentals, practical applications, examples.* Berlin: Springer, 1984.
5. Prior PF, Maynard DE. *Monitoring cerebral function. Long-term monitoring of EEG and evoked potentials.* Amsterdam: Elsevier, 1986.
6. Nuwer MR. *Evoked potential monitoring in the operating room.* New York: Raven Press, 1986.
7. Rosen M, Lunn JN, eds. *Consciousness, awareness, pain and general anaesthesia.* London: Butterworths, 1987.
8. Møller AR. *Evoked potentials in intraoperative monitoring.* Baltimore: Williams and Wilkins, 1988.
9. Grundy BL, Villani RM, eds. *Evoked potentials. Intraoperative and ICU monitoring.* Vienna: Springer Verlag, 1988.
10. Newton DEF, Thornton C, Creagh-Barry P, Dore CJ. Early cortical auditory evoked response in anaesthesia: comparison of the effects of nitrous oxide and isoflurane. *British Journal of Anaesthesia* 1989; **62:** 61–5.
11. International Federation of Societies for Electroencepahalography and Clinical Neurophysiology. *Recommendations for the practice of clinical neurophysiology: methodology for monitoring during anesthesia/surgery and for monitoring during coma.* Amsterdam: Elsevier, 1989 (in press).
12. Andreassen S, Stalberg E. Knowledge-based systems and EMG. In: Desmedt J, ed. *Computer-aided surface and needle electromyography and expert systems in diagnosis.* Amsterdam: Elsevier, 1989 (in press).
13. Andreassen S, Jensen FV, Andersen, Falck B, Kjaerulff U, Woldby M, Sørensen AR, Rosenfalck A, Jensen F. Munin — an expert assistant. In: Desmedt J, ed. *Computer-aided surface and needle electromyograph and expert systems in diagnosis.* Amsterdam: Elsevier, 1989 (in press).
14. Woldbye M, Sørensen AR, Rosenfalck A, Jensen FV, Falck B, Andreassen S. An interactive neuroanatomical knowledge base for EMG. In: Desmedt J, ed. *Computer-aided surface and needle electromyography and expert systems in diagnosis.* Amsterdam: Elsevier, 1989 (in press).

---

## Editorial notices

### Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979: **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

*Anaesthesia*, 1989, Volume 44, pages 547–550

# Anaphylaxis to latex during surgery

F. LEYNADIER, C. PECQUET AND J. DRY

**Summary**

*Five young women, all of whom had anaphylactic responses in operating units, are described. Three of them worked in a hospital, three showed immediate hypersensitivity to fruit and all had known urticaria to latex. Anaphylaxis appeared progressively 15 to 30 minutes after injection of anaesthetic drugs. Skin tests with these drugs were negative. Skin prick tests through gloves and with four different allergen preparations (saline which had been incubated with gloves and three kinds of latex) were positive. Human basophil degranulation tests with all four allergens were positive and radio allergo sorbent tests to latex were also positive. IgE-dependent allergy to latex may be investigated by questionnaire and if necessary by prick tests before each operation to prevent anaphylaxis due to surgical gloves.*

**Key words**

*Allergy*; anaphylaxis, latex.

Urticaria to latex from *Hevea brasiliensis* is well documented and occurs mainly with rubber gloves.[1–5] Recently, Axelsson *et al.*[6] reported five cases of IgE-mediated anaphylactoid reactions to rubber; one of these happened when a gynaecologist used rubber gloves for a vaginal examination. Two cases of anaphylaxis to latex occurred during surgery and were reported briefly by Turjanmaa *et al.*[7] We observed five cases of anaphylaxis due to latex during surgery in 1987. They represent about 10% of patients seen during the same period for a true anaphylaxis to anaesthetic drugs (43 patients).

## Patients and methods

### *First patient*

A 32-year-old woman, who worked as a clerk, was previously anaesthetised three times without any side effects; the last time was one month before for a salpingoscopy. She had had an immediate allergy to foods for at least 10 years; this appeared as urticaria and abdominal pain less than 30 minutes after bananas or avocado pears were eaten. Her skin prick tests (SPT) with these fresh fruits were clearly positive. She suffered for 3 years from urticaria which started about 10 minutes after donning rubber gloves.

A salpingoplasty under general anaesthesia was planned. Premedication was with atropine, hydroxyzine and betamethasone. A urethral latex probe was placed by a nurse who wore latex gloves.

There was an anaphylactic reaction 15 minutes later with angio-oedema, urticaria, wheezing and, within a few minutes, collapse and cyanosis. She was treated successfully with adrenaline and synthetic gelatins (Plasmion).

Anaesthesia was not induced. She was tested in our department 15 days later with intradermal skin tests (IST), as is our routine in cases of anaphylaxis to general anaesthetics,[8] with 13 drugs including the three suspected drugs. ISTs were negative and the diagnosis of allergy to latex was not confirmed. These ISTs were again negative one month later.

She was premedicated 3 months later with intramuscular diazepam and a urethral probe was placed: she again had an anaphylactic response and received the same treatment. One week later the diagnosis of anaphylaxis to latex was finally confirmed: the SPT and radio allergo sorbent skin test (RAST) was positive. The human basophil degranulation test (HBDT) was negative (Tables 1 and 2).

### *Second patient*

A 29-year-old woman who worked as an accountant was previously anaesthetised three times without any side effects; the last time was 2 years earlier. She had had atopic dermatitis and asthma in childhood; later, urticaria and angio-oedema, due probably to drugs (indomethacin) and foods (uncertain) developed. She had no allergy to fruit. Her SPT with 40 foods were negative except for pears (5–15 mm) but this fruit was well tolerated. Urticaria, in response to the use of rubber gloves, occurred within 5–10 minutes for the first time a year earlier. She had a spinal anaesthetic for a Caesarean section with bupivacaine, and an infusion

---

F. Leynadier, MD, J. Dry, MD, Professors, C. Pecquet, MD, Hôpital Rothschild, 33, Bld de Picpus, 75012 Paris, France.
Accepted 30 December 1988.

0003–2409/89/070547+04 $03.00/0
© 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Results of skin tests. Allergen concentration was 1 in 1000 vol/vol throughout, except for tests marked with an asterisk, when it was 1 in 100 vol/vol.

| Prick test | Results (mm) | Patients | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Through glove | Wheal | 8 | 7 | 5 | 10 | 7 |
| | Flare | 40 | 25 | 15 | 40 | 28 |
| Glove supernatant | Wheal | 4 | not done | 0 | 2 | 5 |
| | Flare | 25 | | 0 | 10 | 10 |
| Prevulcanized latex | Wheal | 6 | 5 | 5 | 5 | 5* |
| | Flare | 50 | 22 | 34 | 40 | 28 |
| Latex Latz | Wheal | 9 | 7 | 6 | 7 | 12* |
| | Flare | 45 | 34 | 15 | 40 | 40 |
| Latex HA | Wheal | 7 | 6 | 5 | 4 | 5* |
| | Flare | 40 | 20 | 20 | 30 | 30 |

of synthetic gelatin (Plasmion), ephedrine (10 mg in 2 minutes) and dexamethasone (8 mg) was started.

The baby was delivered and the patient received oxytocin. She developed pruritus and urticaria about 5 minutes later and then cardiovascular collapse. Ephedrine was injected (electric syringe) and hydrocortisone (100 mg intravenously). The pruritus increased, despite ephedrine and hydrocortisone, and angio-oedema and bronchospasm appeared. She was treated successfully with adrenaline and was tested in our department 10 months later. IST to drugs, including bupivacaine and oxytocin, were negative. SPT, HBDT and RAST for latex were positive (Table 1).

### *Third patient*

A 30-year-old nurse was anaesthetised 11 years ago without side effects. She had suffered immediate allergy to rubber gloves for 6 years, but had no allergy to foods. She was anaesthetised for oophorectomy with thiopentone, vecuronium, flunitrazepam and dextromoramide and developed progressive urticaria about 20 minutes later during the operation and then cardiovascular collapse. Adrenaline and hydrocortisone were used successfully and the operation was finished. Two months later IST to drugs were negative. SPT, HBDT and RAST for latex were positive (Table 1).

### *Fourth patient*

A 32-year-old nurse was anaesthetised for the first time 7 years previously without side effects. She had had an allergy to foods for 4 years: urticaria and (or) anaphylaxis to mussels, sweet-peppers and passion-fruit. Her SPT were positive for these foods.

She had had asthma in response to formaldehyde for the last 3 years and allergy to latex gloves for 5 years (urticaria within 10 minutes). She was anaesthetised for cholecystectomy and received thiopentone and pancuronium without side effects. Progressive wheezing, bronchospasm, urticaria and collapse developed over 5–10 minutes when the surgeon's hands were in the abdominal cavity. She received successfully the same treatment as in the first case. The operation was then finished. One month later, IST with anaesthetic drugs were negative. SPT, HBDT and RAST for latex were all positive (Tables 1 and 2).

### *Fifth patient*

A 28-year-old assistant nurse had a general anaesthetic in 1980 and a spinal anaesthetic with bupivacaine one year later for a Caesarean section without side effects. She had had a food allergy (bananas, tomatoes, grapes, pineapples, fish and shellfish) for 5 years. These allergies were confirmed by SPT in our department. For 2 years she had suffered allergy to latex gloves with extensive immediate local urticaria. Conjunctivitis and rhinitis appeared when she rubbed her eyelids when wearing gloves. She received a spinal anaesthetic for another Caesarean section with bupivacaine, and 10 minutes later an injection of oxytocin and dextromoramide was given. The delivery was completed, but about 10 minutes after the injection of drugs she developed angio-oedema of the face, then bronchospasm and collapse. Treatment with adrenaline, hydrocortisone, oxygen and salbutamol spray was successful. Three months later IST to drugs were negative. SPT, HBDT and RAST for latex were positive (Tables 1 and 2).

## Immunological studies

The five patients were tested with the same protocol.

### *Skin prick tests*

Skin prick tests (SPT) were carried out with disposable needles (Stallerpoint, Laboratoire des Stallergènes, 94264 Fresnes, France). Wheal and flare were measured 20 minutes later. Negative (saline solution) and positive (codeine phosphate 9%) controls were used.

There were five challenges used for each patient. Solu-

**Table 2.** Results of HBDT and IgE. Concentration of antigen in parentheses.

| Human basophil degranulation test. Two maximum degranulation values | | Patients | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Glove supernatant | 1 | 0 ($10^{-6}$) | 79 ($10^{-6}$) | 50 ($10^{-4}$) | 38 ($10^{-7}$) | 60 ($10^{-5}$) |
| | 2 | 18 ($10^{-7}$) | 57 ($10^{-7}$) | 60 ($10^{-5}$) | 10 ($10^{-6}$) | 54 ($10^{-6}$) |
| Prevulcanised latex | 1 | 64 ($10^{-6}$) | 81 ($10^{-5}$) | 93 ($10^{-9}$) | 54 ($10^{-8}$) | 54 ($10^{-6}$) |
| | 2 | 60 ($10^{-7}$) | 73 ($10^{-6}$) | 95 ($10^{-10}$) | 58 ($10^{-10}$) | 50 ($10^{-7}$) |
| Latex Latz | 1 | 51 ($10^{-6}$) | 75 ($10^{-5}$) | 86 ($10^{-5}$) | 44 ($10^{-8}$) | 48 ($10^{-5}$) |
| | 2 | 47 ($10^{-7}$) | 76 ($10^{-6}$) | 76 ($10^{-6}$) | 54 ($10^{-9}$) | 64 ($10^{-6}$) |
| Latex HA | 1 | 40 ($10^{-6}$) | 83 ($10^{-5}$) | 80 ($10^{-8}$) | 58 ($10^{-8}$) | 68 ($10^{-5}$) |
| | 2 | 32 ($10^{-7}$) | 70 ($10^{-6}$) | 58 ($10^{-9}$) | 52 ($10^{-9}$) | 68 ($10^{-6}$) |
| Total IgE (iu/ml) | | 136 | 561 | 313 | 1664 | 225 |
| Class of specific IgE | | 2 | 2 | 3 | 3 | 2 |

tions were pricked into the skin through *commercial surgical gloves* (Assistance Publique, Paris).

A *supernatant of a surgical glove* (about 20 g) maintained, after washing with distilled water, in 180 ml of saline at laboratory temperature for 3 hours. Dilutions of 1 in 100 and 1 in 1000 were made in saline.

A *commercial prevulcanised latex* diluted in saline at 1 in 100 and 1 in 1000 (vol/vol). (This kind of latex is generally used in the manufacture of surgical gloves.)

A *commercial nonprevulcanised latex*, low-ammonia TZ 60% (Latz) that contained diammonium phosphate, ammonium laurate, tetramethyl thiurame disulphur and zinc oxide, diluted at 1 in 100 and 1 in 1000 in saline (vol/vol).

A *commercial latex high ammonia 60%* (HA) containing approximately the same chemical products; it was diluted at 1 in 100 and 1 in 1000 (vol/vol).

Three groups of control subjects were skin tested with the same protocol. All had a negative history for immediate allergy to latex. There were 72 patients (32 men) referred for skin tests to general anaesthetics before anaesthesia (29 patients) or after anaphylaxis to anaesthetic drugs (43 patients). Twenty-seven asthmatic patients (14 men) were simultaneously skin tested with 12 inhalant allergens; 17 patients (10 men) were skin tested with food allergens for urticaria (eight cases), angio-oedema (seven cases), or anaphylaxis (two cases).

### *Human basophil degranulation tests*

Human basophil degranulation tests (HBDT) were performed as previously reported[9] (commercially available Allergolam technique Diagnostic Pasteur, Marnes la Coquette 92430, France). The method in brief is as follows. Ten millilitres of blood drawn on EDTA were mixed with 10 ml of Hepès buffer without $Ca^{++}$ and $Mg^{++}$ and deposited on a density medium (1.080 g/ml) and centrifuged (400 g, 30 minutes). The buffy coat was washed once in Hepès buffer. The supernatant was discarded. Twenty microlitres of this suspension enriched in basophils was added to each well of a 10-well slide containing either 20 $\mu$l of Hepès buffer with $Ca^{++}$ and $Mg^{++}$ (final concentration on slide: 2.30 mmol/litre and 1 mmol/litre) or 20 $\mu$l of the antigen diluted with the same buffer. Eight concentrations ($10^{-3}$ to $10^{-10}$) of antigens were studied in duplicate. The slide was dried, fixed and stained with a toluidine blue solution and, finally, mounted after 15 minutes at 37°C.

The basophils were counted on 10 microscopic fields randomly distributed in each well. Basophils are not distinct from the other white cells due to loss of the stained granules after degranulation. The number of basophils counted in control wells was always more than 100. The percentage of degranulation was expressed as:

$$\frac{\text{basophils in control wells—observable basophils in allergen wells}}{\text{basophils in control wells}} \times 100$$

A ratio of 35% was considered positive.[10] The same antigens as above for SPT were used except that they were diluted in Hepès buffer with $Ca^{++}$ and $Mg^{++}$. In a recent study this HBDT procedure proved to be as sensitive as the histamine release test.[11]

HBDT was carried out in five control subjects whose skin tests to latex were negative.

### *Total and specific immunoglobulin*

The commercially available Phadezym technique (Pharmacia France) was used.

## Results

There were no false negative results with control skin tests (saline and codeine) in patients or control subjects.

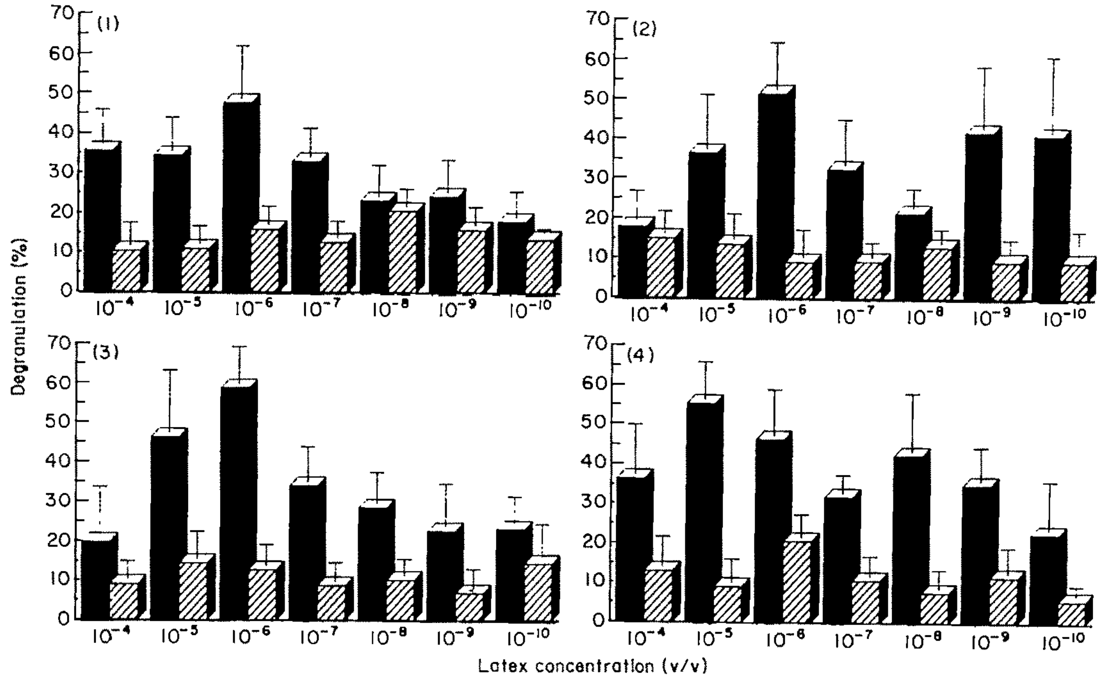


Fig. 1. Mean (SEM) of degranulation observed in five patients (■) and in five control subjects (▨) with the four kinds of latex (see Immunological studies section). 1, glove supernatant; 2, prevulcanised latex; 3, latex Latz; 4, latex HA.

The skin tests with gloves and the four different latex were negative in the 116 control subjects. The percentage degranulation was always less than 35% in the five control subjects studied by HBDT. The mean (SEM) of degranulation values of these five subjects are shown in Figure 1. All results for the five patients appear in Tables 1 and 2. The mean (SEM) of values for degranulation are shown in Figure 1.

## Discussion

It is well known that glove material, especially rubber, can cause allergic eczema. This is mainly due to the chemical products added in the manufacturing process. Estlander *et al.*[1] reported that 12.5% of contact dermatitis is caused by rubber or plastic gloves.

The first case of contact urticaria to latex was published by Nutter[12] but there are many other cases.[1,5,13] Two cases of anaphylactoid reactions due to surgeon's gloves were presented at a congress.[7] In 1987, Axelsson *et al.*[6] reported five cases of IgE-mediated reactions to rubber. We have observed five cases of anaphylaxis to latex in surgeon's gloves in one year. These patients were referred to our department with a false diagnosis of anaphylaxis to anaesthetic drugs. They represent about 10% of the total number of true anaphylactic reactions seen to these drugs over the same period.

Anaesthetic drugs can be excluded because of a number of features in the reactions. There is a delay of at least 15 minutes between the injection of the drugs and the appearance of the signs of anaphylaxis. These signs become progressively worse over a period of 5–10 minutes. Skin testing for the drugs is negative despite the well-known sensitivity to these tests.[8]

The IgE-mediated allergy to latex is obvious and is confirmed by a history of urticaria to rubber gloves and positive SPT, HBDT and RAST. Nurses and doctors are frequently allergic to latex; three of our five patients were working in hospital. The highest prevalence of latex immediate allergy is amongst the staff of operating departments;[13] 7.5% of 54 doctors and 5.6% of 71 nurses compared with 1.3% of 79 other hospital employees and 0.8% of 130 control subjects.

The diagnosis of contact urticaria to latex is difficult: many patients suspected the glove powder (such as case 5), but this aetiology cannot hold when skin tests with natural latex or RAST to latex are positive. The hypothesis that the allergen may be water-soluble proteins is supported by numerous observations. The water-soluble substances obtained after maintaining latex in water give positive skin test and a positive reaction to ninhydrin;[4,5] cyanogen bromide-activated discs used for coating allergen can only bind proteins[5,6] in the RAST technique.

Immunological basophil degranulation cannot be caused by monovalent haptens such as low molecular weight chemical products added to natural latex. Moreover, we observed a highly significant degranulation by using 'glove supernatant' after extensive dialysis against distilled water; this degranulation was totally inhibited by EDTA at $3.10^{-2}$M (unpublished results). A, 12 000–15 000 dalton, protein seems to be the allergenic part of latex, as observed in some preliminary results using an immunoblotting technique. It would be interesting to characterise this (or these) protein (s) and eventually to try specific immunotherapy. It is obvious that a relatively large amount of water-soluble antigen is obtained from a surgical glove. Positive SPT and HBDT were obtained with similar concentrations of glove supernatant as with the commercial latex used for glove manufacture. Atopic disease was frequently observed with latex urticaria in previous reports, but food allergy was not mentioned. Three out of five patients were clearly allergic to different fruits in the present study. It may be possible that cross-allergenicity exists between proteins from latex and some fruits, as is reported to occur between birch pollen and apples.[14]

In conclusion, anaphylaxis to latex gloves is probably more frequent than previously thought: in the few months after the first positive diagnosis, we were able to find four other cases. It is advisable to consider this diagnosis in all unexplained cases of anaphylaxis which occur during operations. Finally, it appears important to detect allergy to latex by questioning patients and, if necessary, by SPT before each operation to prevent anaphylaxis to surgical gloves.

## Acknowledgment

All the latex materials were kindly supplied by J.M. Hetier, Safic-Alcan, 92506 Puteaux, France.

## References

1. Estlander T, Jolanki R, Kanerva L. Dermatitis and urticaria from rubber and plastic gloves. *Contact Dermatitis* 1986; **14:** 20–5.
2. Forstrom L. Contact urticaria from latex surgical gloves. *Contact Dermatitis* 1980; **6:** 33–4.
3. Frosch PJ, Wahl R, Bahmer FA, Maasch HJ. Contact urticaria to rubber gloves is IgE-mediated. *Contact Dermatitis* 1986; **14:** 241–5.
4. Meding B, Fregert S. Contact urticaria from natural latex gloves. *Contact Dermatitis* 1984; **1:** 52–3.
5. Wrangsjo K, Mellstrom G, Axelsson G. Discomfort from rubber gloves indicating contact urticaria. *Contact Dermatitis* 1986; **15:** 79–84.
6. Axelsson JGK, Johansson SGO, Wrangsjo K. IgE-mediated anaphylactoid reactions to rubber. *Allergy* 1987; **42:** 46–50.
7. Turjanmaa K, Reunala T, Tuimala R, Karkkainen T. Severe IgE-mediated allergy to surgical gloves. Proceedings from XV Nordic Congress of Allergology. *Allergy* 1984; **39** (Suppl. 2): abstract No. 35.
8. Leynadier F, Sansarricq M, Didier JM, Dry J. Prick tests in the diagnosis of anaphylaxis to general anaesthetics. *British Journal of Anaesthesia* 1987; **59:** 683–9.
9. Leynadier F, Luce H, Dry J. Méthodologie simplifiée du test de dégranulation des basophiles humains. *Revue Française Allergologie* 1981; **21:** 173–5. Simplified method for the test of degranulation of human basophiles (English title).
10. Dry J, Leynadier F, Luce H. Le test de dégranulation des basophiles humains: comparaison avec les tests cutanés aux pollens de graminées chez 72 sujets. *Annales d'Immunologie* (Paris) 1979; **130C:** 39–48. Correlation of skin test to grass pollen with human basophil degranulation test; results in 72 patients (English title).
11. Vuitton DA, Bresson-Hadni S, Lenys D, Flausse F, Liance M, Wattre P, Miguet JP, Capron A. IgE-dependent humoral immune response in Echinococcus multilocularis infection: circulating and basophil-bound specific IgE against Echinococcus antigens in patients with alveolar echinococcosis. *Clinical and Experimental Immunology* 1988; **71:** 247–52.
12. Nutter AF. Contact urticaria to rubber. *British Journal of Dermatology* 1979; **101:** 597–8.
13. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987; **17:** 270–5.
14. Lahti A, Bjorksten F, Hannuksela M. Allergy to birch pollen and apple, and cross-reactivity of the allergens studied with the RAST. *Allergy* 1980; **35:** 297–300.

*Anaesthesia*, 1989, Volume 44, pages 551–554

# The pressor response and laryngeal mask insertion

## A comparison with tracheal intubation

N. BRAUDE, E. A. F. CLEMENTS, U. M. HODGES AND B. P. ANDREWS

**Summary**

*The pressor response associated with laryngoscopy and tracheal intubation may be harmful to certain patients. The laryngeal mask airway avoids the need for laryngoscopy and allows positive pressure ventilation of the lungs in appropriate patients. This study compared the pressor response of tracheal intubation with that of mask insertion in two groups of 24 and 23 healthy patients respectively. All patients were anaesthetised with thiopentone, nitrous oxide, enflurane and paralysed with atracurium. We have shown a similar, but attenuated pattern of response associated with mask insertion in comparison with laryngoscopy and intubation; significant differences between the groups were evident in arterial diastolic blood pressure immediately after insertion and again 2 minutes later. Use of the laryngeal mask may therefore offer some limited advantages over tracheal intubation in the anaesthetic management of patients where the avoidance of the pressor response is of particular concern.*

**Key words**

*Blood pressure*; hypertension.
*Intubation, tracheal*; laryngeal mask.

The pressor response to tracheal intubation may be harmful to patients with ischaemic heart disease, hypertension or cerebrovascular disease.[1] Attempts are made to attenuate this response with a variety of pharmacological manoeuvres[2] and more recently the effect of fibreoptic laryngoscopy was investigated.[3] The laryngeal mask airway has recently become commercially available (manufactured and distributed by Colgate Medical Ltd). It does not offer airway protection against foreign material in the pharynx, but it does provide adequate airway control to allow intermittent positive pressure ventilation.[4] The cardiovascular responses to the insertion of this device have not previously been investigated.

Both experimental and clinical evidence suggests that pharyngeal wall stimulation associated with laryngoscopy is the major cause of the pressor response.[5,6] This study examined the pressor response associated with laryngeal mask insertion, since the laryngeal mask avoids the need for laryngoscopy, and compared this with laryngoscopy and tracheal intubation in anaesthetised, fit patients.

## Methods

Hospital ethics committee approval for the study was obtained. Patient consent was not requested because the laryngeal mask is used interchangeably with tracheal tubes in our hospital in appropriate circumstances.

Fifty fit adult patients (ASA 1) who presented for elective surgery and required artificial ventilation of the lungs were studied. All patients were premedicated with lorazepam 0.05 mg/kg orally 2 hours before operation. Intravenous access was established after arrival in the anaesthetic room; continuous ECG monitoring and pulse oximetry were then commenced and arterial pressure and heart rate recorded every minute thereafter using a Dinamap 1846 oscillotonometric blood pressure monitor.

Baseline readings were recorded, after a stabilisation period of 5 minutes, and anaesthesia induced with thiopentone 4–6 mg/kg intravenously (until the eyelash reflex was lost). This was followed by 2 ml of normal saline and then atracurium 0.6 mg/kg injected over 15 seconds. The lungs were then ventilated manually through a Bain system and facemask with 66% nitrous oxide and 1.0% enflurane in oxygen. The first arterial blood pressure and pulse rate readings were recorded one minute after induction, after which an oral airway was inserted. Readings were thereafter recorded each minute for the subsequent 4 minutes. End-tidal carbon dioxide was sampled from beneath the facemask and measured using an Engström Eliza end-tidal carbon dioxide analyser, which maintained levels between 4.5% and 5.0%. The patients were then randomly allocated to either the intubation or laryngeal mask group.

---

N. Braude, MB, ChB, MRCP, FFARCS, Senior Registrar, E.A.F. Clements, MB, BS, FFARCS, Consultant, U.M. Hodges, BSc, MB, BS, DA, Registrar, B.P. Andrews, Principal ODA, Department of Anaesthesia, Whipps Cross Hospital, Leytonstone, London E11 1NR.
Correspondence to be addressed to Dr N. Braude, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE.
Accepted 20 January 1989.

0003–2409/89/070551+04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

Tracheal intubation was performed using a Macintosh laryngoscope, or the laryngeal mask was inserted blindly by the technique recommended by the manufacturers. A size 8.0 or 9.0 tracheal tube, in women and men respectively (Vygon series 521), or a size 3 laryngeal mask, in both men and women (Intavent laryngeal mask airway) lubricated with KY jelly, was used by the same experienced anaesthetist (E.A.F.C.). Air was injected into the tracheal tube cuff or the laryngeal mask cuff until a seal was achieved. The time taken from removal of the facemask to reconnexion of the catheter mount was recorded. Positive pressure ventilation was continued by hand using a Bain system with end-tidal carbon dioxide concentrations sampled via a catheter from approximately 10 cm above laryngeal level in both groups. Levels were maintained between 4.75% and 5.25%. Arterial blood pressure and heart rate were recorded for the next 5 minutes.

All patients were questioned 24 hours after surgery as to whether they had experienced a sore throat in the postoperative period. Patients were not studied if any abnormal cardiac rhythm developed, if intubation or mask insertion took longer than 40 seconds to accomplish or if the oxyhaemoglobin saturation decreased to below 90% after induction.

Data were analysed using unpaired Student's *t*-tests and Chi-squared analysis with Yates' correction. Results are quoted as mean (SEM) and statistical significance was assumed at $p < 0.05$.

## Results

Three patients were removed from the study because they developed nodal arrhythmia, oxyhaemoglobin desaturation or because of difficulty in tracheal intubation. Twenty-four of the remaining patients were allocated to the tracheal group and 23 to the laryngeal mask group; no difficulties were experienced in positioning the mask or achieving a seal. There were no significant differences in demographic detail between the groups (Table 1).

There was no significant difference between the groups before intubation or mask insertion in respect of pulse rate or blood pressure. Both groups exhibited a significant increase in pulse rate in the first 3 minutes after induction and a significant decrease in systolic blood pressure 5 minutes after induction; the laryngeal mask group also demonstrated a significant decrease in diastolic blood pressure after 5 minutes.

There was a significant increase in systolic blood pressure immediately after tracheal intubation and for the subsequent 2 minutes (maximum mean increase 17.1%). Diastolic blood pressure (maximum mean increase 26.8%) and pulse rate (maximum mean increase 13.2%) were similarly elevated immediately after intubation and for the next minute's reading.

**Table 1.** Details of participating patients.

| | Tracheal tube | Laryngeal mask |
|---|---|---|
| Number of patients | 24 | 23 |
| Weight, kg, mean | 66.9 (2.11) | 68.7 (2.73) |
| 10th centile | 55 | 57 |
| 90th centile | 80 | 88 |
| Age, years, mean | 40.5 (2.53) | 36.1 (2.37) |
| 10th centile | 25 | 25 |
| 90th centile | 56 | 55 |
| Sex ratio (M:F) | 0.37:1 | 0.3:1 |

Mask insertion, in the laryngeal mask group, was associated with a systolic increase that achieved significance at one minute after insertion (8.6% mean rise). Diastolic blood pressure was significantly elevated immediately after insertion and for the next minute (maximum mean increase 11.8%), while heart rate increased significantly only immediately after mask insertion (13.1% mean increase).

Significant differences between the two groups occurred in diastolic blood pressure. There was a 14.2% greater increase in diastolic pressure in the intubated patients immediately after intubation or mask insertion, and 2 minutes later a 8.9% greater increase. Differences in systolic blood pressure did occur (17.1% increase compared to 8.6% initial increase), but these did not achieve significance. Heart rate changes were similar in both groups.

Mean time taken to intubate or insert the laryngeal mask was significantly shorter in the laryngeal mask group [17.0 (1.53) seconds] than the intubated group [22.2 (1.46) seconds]. One of the intubated patients and five in the mask group complained of a sore throat postoperatively. This difference was not significant.

## Discussion

Insertion of the laryngeal mask was clearly associated with an increase in both blood pressure and heart rate in this study of healthy patients who had elective surgery. Pulse rate increases are similar, compared with laryngoscopy and tracheal intubation, but the increase in mean blood pressure is both attenuated and of a shorter duration.

The increases in systolic and diastolic arterial blood pressure associated with mask insertion were proportionately similar (but on a smaller scale) to those that resulted from laryngoscopy and intubation. Mean heart rate changes were not significantly different; the absence of a statistically significant increase in the mask group one minute after insertion (despite a higher mean than the tube group) was due to the greater spread of data.

The pressor response of laryngoscopy and intubation stems largely from pharyngeal wall stimulation due to laryngoscopy, with intubation producing a smaller additional response.[5,6] Insertion of the laryngeal mask does not require a laryngoscope, although introduction of the device and inflation of the cuff stimulates and exerts pressure on the anterior pharyngeal wall. This is almost certainly the mechanism by which the increases in blood pressure and pulse rate occur; the transient nature of the response suggests that this is not related to the continuous pressure exerted by the sealing cuff. The reduced response may reflect the lesser stimulus compared to laryngoscopy, the lack of direct laryngeal and tracheal stimulation or the shorter duration of stimulus that results from quicker insertion.

The reason the mask group exhibited an attenuated blood pressure increase but a virtually identical pulse rate increase is unclear. This may reflect a difference in the pattern of catecholamine output, although previous studies of laryngoscopy and intubation have failed to show a significant correlation between plasma adrenaline concentrations and heart rate.[6,7] It has been postulated that heart rate increases may be a response to an imbalance between

**Table 2.** Mean pressure and pulse rate changes (SEM).

| | | | | | | Systolic blood pressure (mmHg) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Time (minutes) | Control | 1 | 2 | 3 | 4 | 5 | 0 | 1 | 2 | 3 | 4 | 5 |
| Tracheal tube group | 134.4<br>(2.85) | 127.4<br>(3.40) | 134.9<br>(5.00) | 129.6<br>(3.90) | 125.7<br>(3.46) | 122.7*<br>(3.10) | 143.7†<br>(4.48) | 142.1†<br>(3.82) | 133.0†<br>(3.76) | 126.0<br>(3.42) | 118.8<br>(2.80) | 114.5<br>(2.54) |
| Laryngeal mask group | 138.2<br>(3.67) | 125.7<br>(3.87) | 133.3<br>(3.98) | 130.3<br>(4.11) | 129.6<br>(4.52) | 126.9*<br>(3.94) | 136.5<br>(4.35) | 137.8†<br>(3.58) | 129.2<br>(3.56) | 124.2<br>(3.03) | 118.8<br>(2.99) | 116.0<br>(2.88) |
| | | | | | | Diastolic blood pressure (mmHg) | | | | | |
| Time (minutes) | Control | 1 | 2 | 3 | 4 | 5 | 0 | 1 | 2 | 3 | 4 | 5 |
| Tracheal tube group | 77.1<br>(2.14) | 76.7<br>(2.69) | 78.7<br>(2.93) | 74.9<br>(2.74) | 72.7<br>(2.45) | 70.6<br>(2.75) | 89.5†<br>(2.41) | 81.9†<br>(2.22) | 77.2<br>(2.24) | 71.6<br>(2.04) | 66.7<br>(1.98) | 65.4<br>(1.87) |
| Laryngeal mask group | 77.1<br>(1.99) | 73.8<br>(2.60) | 76.1<br>(3.33) | 73.1<br>(2.58) | 71.3<br>(2.75) | 70.1*<br>(2.35) | 78.3†‡<br>(2.53) | 76.0<br>(2.39) | 70.9†‡<br>(1.98) | 67.1<br>(1.93) | 64.2<br>(1.75) | 62.3<br>(1.82) |
| | | | | | | Heart rate (beats/minute) | | | | | |
| Time (minutes) | Control | 1 | 2 | 3 | 4 | 5 | 0 | 1 | 2 | 3 | 4 | 5 |
| Tracheal tube group | 86.1<br>(3.41) | 103.2*<br>(3.87) | 101.0*<br>(3.98) | 95.9*<br>(3.19) | 92.7<br>(3.14) | 91.4<br>(3.36) | 103.5†<br>(2.82) | 100.9†<br>(2.97) | 98.6<br>(3.31) | 95.2<br>(2.97) | 90.7<br>(2.78) | 87.7<br>(2.68) |
| Laryngeal mask group | 86.2<br>(3.69) | 107.9*<br>(4.12) | 105.4*<br>(3.82) | 97.7*<br>(3.60) | 94.6<br>(3.85) | 91.5<br>(3.90) | 103.5†<br>(3.19) | 102.0<br>(3.48) | 96.0<br>(3.38) | 91.4<br>(2.96) | 87.7<br>(2.72) | 85.8<br>(2.87) |

Control refers to the last reading taken before induction and the second set of minute readings to after mask insertion or intubation.
*Significant difference compared with control ($p<0.05$).
†Significant difference compared with last reading before intubation or mask insertion ($p<0.05$).
‡Significant difference compared with tracheal group at this time ($p<0.05$).

vagal and cardiac accelerator fibres,[6] but it seems unlikely that this balance should be similar in both groups.

There was an anecdotal suggestion that the ability to insert the mask smoothly under light general anaesthesia, as well as its excellent tolerance during emergence, may equate with an absent pressor response.[8] The study did not directly address this, but our results do not support this impression. This is not altogether surprising since laryngoscopy produces a greater pressor response than intubation, despite its tolerance by the patient at a much lighter level of anaesthesia. Assessment of the pressor response using indirect blood pressure monitoring may reduce the observed extremes of variation. The nature of the mask however, limits its use to surgery where invasive monitoring is rarely indicated.

The number of patients who experienced sore throats postoperatively did not show significant variation between the groups, although the number of intubated patients with sore throats is smaller than the 10–90% that previous studies have shown.[9] This wide variation emphasises the need for examination of a larger sample if conclusive inferences are to be made about these data.

In conclusion, laryngeal mask insertion in fit patients is associated with an attenuated pressor response in comparison with laryngoscopy and intubation. The laryngeal mask appears more suitable where concern about the pressor response exists given otherwise equal indications for intubation or mask insertion. These results may be applicable to patients with hypertension, ischaemic heart disease and poor left ventricular function, but further work is necessary to confirm this.

## References

1. Prys-Roberts C, Greene LT, Meloche R, Foëx P. Studies of anaesthesia in relation to hypertension II: Haemodynamic consequences of induction and endotracheal intubation. *British Journal of Anaesthesia* 1971; **43:** 531–47.
2. Abou-Madi M, Keszler H, Yacoub O. A method for prevention of cardiovascular reactions to laryngoscopy and intubation. *Canadian Anaesthetists' Society Journal* 1975; **22:** 316–29.
3. Smith JE. Heart rate and arterial pressure changes during fibreoptic tracheal intubation under general anaesthesia. *Anaesthesia* 1988; **43:** 629–32.
4. Brain AIJ. The laryngeal mask—a new concept in airway management. *British Journal of Anaesthesia* 1983; **55:** 801–5.
5. Tomori Z, Widdicombe JD. Muscular, bronchomotor and cardiovascular reflexes elicited by mechanical stimulation of the respiratory tract. *Journal of Physiology* 1969; **200:** 25–49.
6. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. *British Journal of Anaesthesia* 1987; **59:** 295–9.
7. Derbyshire A, Chmielewski A, Fell D, Vater D, Achola K, Smith G. Plasma catecholamine responses to tracheal intubation. *British Journal of Anaesthesia* 1983; **55:** 855–9.
8. Alexander CA, Leach AB, Thompson AR, Lister JB. Use your Brain! *Anaesthesia* 1988; **43:** 893–4.
9. Patrick MR. Airway manipulations. In: Taylor TH, Major E, eds. *Hazards and complications of anaesthesia.* Edinburgh: Churchill Livingstone, 1987; 349.

*Anaesthesia,* 1989, Volume 44, pages 555–558

# A double-blind comparison of epidural ketamine and diamorphine for postoperative analgesia

S. J. PEAT, P. BRAS AND M. H. HANNA

## Summary

*Twenty patients who had abdominal hysterectomy under general anaesthesia were randomly assigned to receive either epidural ketamine (30 mg), or epidural diamorphine (5 mg) peri-operatively and on first request for analgesia. Failure to obtain satisfactory analgesia with one of the agents was treated by epidural administration of the other. Pain was assessed by an independent observer, and by the patient using a visual analogue scale. The mean (SD) pain score on recovery from general anaesthesia, on a scale of 0–4, was 2.9 (1.2) for the ketamine group and 1.0 (1.0) for the diamorphine group ($p < 0.01$). The mean (SD) time to first request for analgesia was 272 (206) and 72 (41) minutes in the diamorphine and ketamine groups respectively ($p < 0.01$). All patients in the diamorphine group obtained adequate analgesia, but all patients in the ketamine group were changed to epidural diamorphine. Epidural ketamine does not appear to be a sufficiently effective alternative to epidural diamorphine for routine use in postoperative pain.*

**Key words**

*Analgesics*; ketamine, diamorphine.
*Anaesthetic techniques*; epidural.

Spinal opiates, although superior to systemic opiates in the control of postoperative pain, have the potential to produce serious side effects, particularly respiratory depression.[1] The phencyclidine derivative ketamine was investigated as a postoperative analgesic and shown, in an open trial, to be more effective epidurally than intramuscularly at doses of 30 mg.[2] Initial reports of the use of epidural ketamine at a lower dose were encouraging, and suggested that 4 mg gave adequate postoperative pain relief for 4 hours after lower abdominal and lower limb surgery.[3] However, a study which investigated the duration of postoperative analgesia demonstrated that in major gynaecological surgery epidural ketamine in doses of up to 8 mg is inferior to epidural morphine and no more effective than placebo.[4]

The present double blind study compares the efficacy of high dose epidural ketamine with that of epidural diamorphine for control of pain after abdominal hysterectomy.

## Methods

Twenty patients (ASA 1 or 2) between the ages of 25 and 70 years, having elective abdominal hysterectomy were studied. Patients with spinal abnormalities, significant renal, cardiovascular, hepatic or psychiatric disorders were excluded. The protocol received hospital ethics committee approval and each patient gave written informed consent. The patients were instructed in the use of a 10-cm visual analogue scale on the evening prior to surgery and told to request analgesia at any time postoperatively when more than slight pain occurred.

Premedication was with oral temazepam 20 mg 1–2 hours before operation. Anaesthesia was induced with etomidate 0.25–0.3 mg/kg and fentanyl 3 μg/kg. Muscle relaxation was provided with atracurium and anaesthesia maintained with nitrous oxide, oxygen and isoflurane. An epidural catheter was inserted after induction of anaesthesia at the $L_{1/2}$ or $L_{2/3}$ interspace, using a loss of resistance technique, and threaded 3 cm cranially.

The patients were randomly assigned to receive either ketamine (30 mg) or diamorphine (5 mg) injected into the epidural space in a volume of 3 ml at the start of peritoneal closure. The administration of isoflurane was stopped on skin closure and muscle relaxation reversed. Assessments were made by an independent observer on recovery and at 1, 2, 4, 6, 8 and 24 hours after operation. Respiratory rate, blood pressure, and pulse rate were noted at each visit. Pain was evaluated by the patient using a 10-cm visual analogue scale and by the observer as absent, slight, moderate, severe or very severe. Side effects (nausea, vomiting, itching, headache and nightmares) were assessed by direct questioning.

---

S.J. Peat, BSc, FFARCS, Research Fellow, P. Bras, FFARCS, Senior Registrar, M.H. Hanna, FFARCS, Consultant Pain Relief Unit, Department of Anaesthesia, Kings College Hospital, Denmark Hill, London SE5 7RH.

Accepted 20 December 1988.

0003–2409/89/070555+04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Patient characteristics and duration of procedures.

| Group | $n$ | Age, years, mean (SD) | Weight, kg, mean (SD) | Height, cm, mean (SD) | Anaesthesia,* minutes, mean (SD) | Closure,† minutes, mean (SD) |
|---|---|---|---|---|---|---|
| Ketamine | 10 | 45.8 (12.5) | 66.2 (16.0) | 154.1 (7.5) | 86.9 (16.8) | 10.1 (4.0) |
| Diamorphine | 10 | 42.8 (5.0) | 69.6 (18.4) | 157.5 (7.5) | 103.5 (26.0) | 10.1 (2.6) |
| Significance | | NS | NS | NS | NS | NS |

*Time from induction to cessation of isoflurane administration.
†Time from epidural injection to cessation of isoflurane administration.
NS, not significant

Differences in pain scores, respiratory rate, blood pressure and duration of analgesia were analysed using the Wilcoxon two sample test. Fisher's exact test was used to compare the incidence of side effects in the two groups.

Epidural analgesia was given according to the following protocol.

*Ketamine group.* Ketamine (30 mg in 3 ml) peri-operatively and at the first request for analgesia. Epidural diamorphine was given if improvement in pain control was not evident within 20 minutes, or the analgesia provided was inadequate.

*Diamorphine group.* Diamorphine (5 mg in 3 ml) peri-operatively and at the first request for analgesia. Ketamine was given if improvement in pain control was not evident within 20 minutes, or the analgesia provided was inadequate epidural.

## Results

Patients in both groups were comparable in terms of weight, height, duration of anaesthesia and time from epidural injection to end of isoflurane (Table 1). Epidural catheters were sited at $L_{2/3}$ in six patients in the diamorphine group and five in the ketamine group; the remainder were at $L_{1/2}$. Surgery was via a transverse lower abdominal incision with the exception of two patients in the ketamine group and one in the diamorphine group, where longitudinal incisions were used.

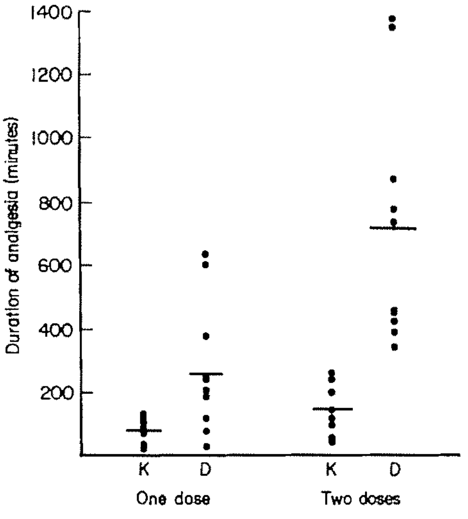


**Fig. 1.** Duration of analgesia following one and two doses of epidural ketamine (30 mg) or diamorphine (5 mg). Bars represent means. K, ketamine group; D, diamorphine group.

### *Assessment on recovery from anaesthesia*

Ten minutes after isoflurane was stopped, all patients could recall their date of birth, and the mean (SD) pain score (scale 0–4) was 1.0 (1) for the diamorphine group and 2.9 (1.2) for the ketamine group ($p < 0.01$). Patients in the diamorphine group had a significantly lower systolic blood pressure, pulse rate and respiratory rate than those in the ketamine group. Vomiting occurred more frequently in the diamorphine group and nausea in the ketamine group but these differences were not statistically significant (Table 2). One patient in the ketamine group appeared to be hallucinating on recovery, but did not subsequently recall this. There was no evidence of obvious motor blockade in any patient.

### *Assessment over postoperative 24 hours*

The mean (SD) time to first request for analgesia was 72.4 (40.8) minutes in the ketamine group and 272.7 (206.4) minutes in the diamorphine group ($p < 0.01$). The mean (SD) duration of analgesia provided by the first two doses of the test drugs was 133 (79) and 718 (385) minutes for the ketamine and diamorphine groups respectively ($p < 0.001$) (Fig. 1). All patients in the ketamine group were switched to diamorphine during the trial (on a double-blind basis) since analgesia provided was suboptimal. Pain scores recorded by those patients still receiving ketamine at 1 and 2 hours postoperatively were significantly higher than those recorded by patients who initially received diamorphine ($p < 0.05$). There was no significant difference between the

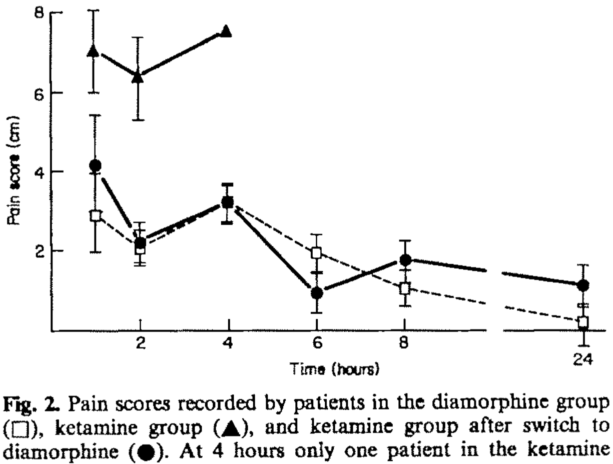


**Fig. 2.** Pain scores recorded by patients in the diamorphine group (□), ketamine group (▲), and ketamine group after switch to diamorphine (●). At 4 hours only one patient in the ketamine group had not been switched to diamorphine.

Table 2. Assessment on recovery.

| Group | *n* | Pain score 0–4,* mean (SD) | Systolic blood pressure mmHg, mean (SD) | Pulse rate beats/minute, mean (SD) | Respiratory rate breaths/minute, mean (SD) | Nausea | Vomiting |
|---|---|---|---|---|---|---|---|
| Ketamine | 10 | 2.9 (1.2) | 145 (25.5) | 78.7 (6.2) | 20.8 (3.1) | 50% | 10% |
| Diamorphine | 10 | 1.0 (1.0) | 125 (14.7) | 66.4 (5.7) | 12.7 (1.8) | 30% | 30% |
| Significance | | $p < 0.01$ | $p < 0.05$ | $p < 0.01$ | $p < 0.01$ | NS | NS |

*Evaluation on a scale of 0–4: 0, nil; 1, slight; 2, moderate; 3, severe; 4, very severe.
NS, not significant.

pain scores recorded by patients in either group (Fig. 2) after the change to diamorphine.

## Discussion

Ketamine has analgesic activity in man at subanaesthetic plasma levels,[5] and analgesia that outlasted the duration of ketamine anaesthesia was observed shortly after the drug's introduction into clinical practice.[6] However, when given postoperatively by the intravenous or intramuscular routes the short duration of action, complex pharmacokinetics, sedative and psychotomimetic effects limit the use of ketamine as an analgesic.[2,5,7,8]

Postulated mechanisms by which ketamine analgesia could be mediated include both central and peripheral sites of action. Ketamine binds stereospecifically to opiate receptors,[9] but a significant contribution to its analgesic efficacy may come from interaction with cholinergic,[10] adrenergic and 5-HT[11] systems.

A direct action of ketamine on the dorsal horn of the transected cat spinal cord has been reported.[12] However, other studies indicate that in decerebrate cats low dose ketamine activates the supraspinal pain inhibition system, and that this indirect mechanism is solely responsible for the ability of ketamine to attenuate the cord's response to bradykinin.[13–15] Ketamine can prevent action potential conduction by an action at sodium and potassium channels in nerve membranes, and hence is considered to have local anaesthetic properties.[16]

A spinal site of action in man is suggested by the production of a distinct sensory level, before the onset of central effects, after intrathecal administration. However, the required dose approaches that needed for intravenous induction of general anaesthesia, and the surgical analgesia produced is of short duration.[17] The local anaesthetic action of ketamine was demonstrated in man by its ability to produce analgesia when used by an intravenous regional technique.[18]

Epidural ketamine in low doses was shown to be inferior to epidural opiates in single blind trials.[4,19] Reports of studies with higher doses for pain control after upper abdominal surgery indicate that epidural ketamine can provide analgesia with an onset time of 20 minutes and duration of 3.8 (1.6) hours (SD) after 15 mg, and analgesia for approximately 17 hours after 30 mg.[2,20] However neither of these studies compared epidural ketamine with opiates.

The results of the present study agree with a number of reports that indicate the lack of efficacy of epidural ketamine at high doses after major surgery,[21,22] and confirm that diamorphine is the more effective agent.

This double-blind controlled study demonstrates the superiority of 5 mg epidural diamorphine over 30 mg epidural ketamine, in terms of both duration and quality of analgesia provided.

## References

1. Rawal N, Arner S, Gustafsson LL, Allvin R. Present state of extradural and intrathecal opioid analgesia in Sweden. A nationwide follow-up survey. *British Journal of Anaesthesia* 1987; **59:** 791–9.
2. Naguib M, Adu-Gyamfi Y, Absood GH, Farag H, Gyasi HK. Epidural ketamine for postoperative analgesia. *Canadian Anaesthetists' Society Journal* 1986; **33:** 16–21.
3. Islas JA, Astorga J, Laredo M. Epidural ketamine for control of postoperative pain. *Anesthesia and Analgesia* 1985; **64:** 1161–2.
4. Kawana Y, Sato H, Shimada H, Fujita N, Ueda Y, Hayashi A, Araki Y. Epidural ketamine for postoperative pain relief after gynecologic operations: a double-blind study and comparison with epidural morphine. *Anesthesia and Analgesia* 1987; **66:** 735–8.
5. Grant IS, Nimmo WS, Clements, JA. Pharmacokinetics and analgesic effects of I.M. and oral ketamine. *British Journal of Anaesthesia* 1981; **53:** 805–9.
6. White PF, Way WL, Trevor AJ. Ketamine—its pharmacology and therapeutic uses. *Anesthesiology* 1982; **56:** 119–36.
7. Owen H, Reekie RM, Clements JA, Watson R, Nimmo WS. Analgesia from morphine and ketamine. A comparison of infusions of morphine and ketamine for postoperative analgesia. *Anaesthesia* 1987; **42:** 1051–6.
8. Austin TR. Ketamine on demand for postoperative analgesia. *Anaesthesia* 1981; **36:** 214.
9. Finck AD, Ngai SH. Opiate receptor mediation of ketamine analgesia. *Anesthesiology* 1982; **56:** 291–7.
10. Wachtel RE. Ketamine decreases the open time of single-channel currents activated by acetylcholine. *Anesthesiology* 1988; **68:** 563–70.
11. Pekoe GM, Smith DJ. Ketamine analgesia: mediation by biogenic amine and endogenous opiate processes. *Anesthesiology* 1979; **51:** S36.
12. Kitahata LM, Taub A, Kosaka Y. Lamina-specific suppression of dorsal-horn unit activity by ketamine hydrochloride. *Anesthesiology* 1973; **38:** 4–11.
13. Tomemori N, Komatsu T, Shingu K, Urabe N, Seo N, Mori K. Activation of the supraspinal pain inhibition system by ketamine hydrochloride. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 355–9.
14. Shingu K, Osawa M, Omatsu Y, Komatsu T, Urabe N, Mori K. Naloxone does not antagonize the anesthetic-induced depression of nociceptor-driven spinal cord response in spinal cats. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 526–32.
15. Mori K, Shingu K. Epidural ketamine does not produce analgesia. *Anesthesiology* 1988; **68:** 296–8.
16. Benoit E, Carratu MR, Dubois JM, Mitolo-Chieppa D. Mechanism of action of ketamine in the current and voltage clamped myelinated nerve fibre of the frog. *British Journal of Pharmacology* 1986; **87:** 291–7.

17. Bion JF. Intrathecal ketamine for war surgery. A preliminary study under field conditions. *Anaesthesia* 1984; **39**: 1023–8.
18. Amiot JF, Bouju PH, Palacci JH, Balliner E. Intravenous regional anaesthesia with ketamine. *Anaesthesia* 1985; **40**: 899–901.
19. Ravat F, Dorne R, Baechle JP, Beaulaton A, Lenoir B, Leroy P, Palmier B. Epidural ketamine or morphine for postoperative analgesia. *Anesthesiology* 1987; **66**: 819–22.
20. Mok MS, Chan KM, Chung SK, Lee TY, Lippmann M. Evaluation of the analgesic effect of epidural ketamine. *Anesthesia and Analgesia* 1987; **66**: S121.
21. Brock-Utne JG, Rubin J, Mankowitz E. Epidural ketamine for control of postoperative pain. *Anesthesia and Analgesia* 1986; **65**: 990.
22. Van der Auwera D, Verborgh C, Camu F. Epidural ketamine for postoperative analgesia. *Anesthesia and Analgesia* 1987; **66**: 1340.

*Anaesthesia*, 1989, Volume 44, pages 559–562

# Effect of single-dose omeprazole on intragastric acidity and volume during obstetric anaesthesia

J. MOORE, R. J. FLYNN, M. SAMPAIO, C. M. WILSON AND K. R. W. GILLON

## Summary

*Various antacid or antisecretory agents are used to reduce the risk to patients of aspiration of gastric contents during general anaesthesia and a trial of the gastric proton pump inhibitor, omeprazole, is reported here. Twenty women admitted for elective Caesarean section under general anaesthesia received a single 80-mg oral omeprazole dose at 2000 hours on the evening before surgery. Intragastric pH and volume were measured immediately after induction of anaesthesia and on completion of surgery. Eighty-five percent of pH measurements at induction and extubation and 80% and 95% of volume measurements at induction and extubation respectively met the defined success criteria ($pH \geq 2.5$, volume $< 25$ ml). Omeprazole treatment was well tolerated by the women and Apgar scores and subsequent progress of the babies were acceptable. These results indicate that gastric acidity and volume were acceptable in the majority of women after omeprazole treatment, but the interval from drug administration to induction of anaesthesia may have been too long in some cases and resulted in unacceptably low pHs.*

## Key words

*Gastrointestinal tract*; stomach, pH.
*Complications*; aspiration.

Acid aspiration during general anaesthesia is associated with considerable morbidity and mortality. In 1946 Mendelson[1] highlighted the problem in pregnancy and suggested that alkalinisation of stomach contents should be carried out in those who required general anaesthesia for delivery. Various methods have been used since then to neutralise the acidity of stomach contents; these include saline and emulsion antacids, anticholinergic drugs and $H_2$ receptor antagonists. The benefit and reliability of any of these drugs is controversial and recent reports suggest that emulsion antacids, given in appropriate doses, provide little or no protection and can themselves cause serious pulmonary complications.[2]

Stimulation of cholinergic, histaminergic and gastrinergic receptors provokes acid secretion from the parietal cells via a common pathway that involves cyclic adenosine monophosphate (cAMP) formation. This activates gastric $H^+K^+$ ATPase, the proton pump of the parietal cell, and omeprazole, a substituted benzimidazole (Fig. 1), blocks this terminal step in the acid secreting pathway.[3] Volunteer studies and investigations in patients with duodenal ulcers or Zollinger–Ellison syndrome have shown that omeprazole in 20–40-mg doses had a long duration of effect and once-daily treatment effectively reduced gastric acidity for 12–24 hours.[3] Serious side effects have not been reported and this concurs with the view that its action at the parietal cell is highly selective. Howden *et al.*[4] reported that omeprazole reduces the volume of gastric juice secreted but not by the same order of magnitude as its effect on acid output.

The concept of a single oral treatment to control gastric acid output and volume during labour is attractive and an investigation into pretreatment with omeprazole in patients who have general anaesthesia for elective Caesarean section seemed to be indicated, firstly to confirm the long duration of suppression of acid secretion and secondly to ascertain the degree of placental transfer. The investigation was approved by the local Medical Ethics Research Committee and informed written consent was obtained from individual patients.

## Methods

Healthy women with an uncomplicated pregnancy of 36 weeks' gestation or more and who were to be delivered by elective Caesarean section under general anaesthesia were

---

J. Moore, MD, PhD, FFARCS, Consultant, R.J. Flynn, MB, BCh, FFARCS, Senior Registrar, M. Sampaio, MB, BCh, FFARCS, Registrar, Department of Anaesthetics, Belfast City Hospital and the Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL, C.M. Wilson, MD, FFARCSI, Consultant, Ulster Hospital, Upper Newtonards Road, Dundonald, Belfast BT16 0RH, K.R.W. Gillon, BSc, PhD, Clinical Projects Manager, Astra Clinical Research Unit, 10 York Place, Edinburgh EH1 3EP.

Accepted 28 November 1988.

0003–2409/89/070559+04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

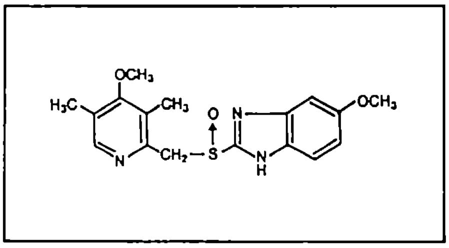


Fig. 1. Structural formula of omeprazole.

selected for the study. They were given, at 2000 hours on the evening before surgery, 80 mg omeprazole orally as gelatin capsules that contained enteric-coated granules, and fasted from 2200 hours. General anaesthesia was induced, using a standard technique, 12–16 hours after omeprazole administration. Anaesthesia was induced with thiopentone 3–5 mg/kg and suxamethonium 100 mg after pre-oxygenation; cricoid pressure was applied throughout until the trachea was securely intubated. Anaesthesia was maintained with 50% nitrous oxide in oxygen, increased at delivery to 66% and supplemented throughout by halothane 0.5%. Neuromuscular blockade was continued with vecuronium 5 mg, reversed at the end of surgery by atropine 1.2 mg and neostigmine 2.5 mg. All patients received alfentanil 1 mg and syntocinon 5 units at delivery. Additional syntocinon was given to promote uterine contraction, if requested. Patients were continuously monitored by ECG, arterial blood pressure, end-tidal $CO_2$ and pulse oximetry.

Stomach contents were aspirated from a Salem sump tube (18 gauge) introduced via a tracheal tube placed in the oesophagus to avoid contamination by oropharyngeal contents, immediately after tracheal intubation and also immediately before extubation. The tube was passed until only the last 10 cm remained visible and the stomach was emptied using a 50-ml syringe attached to the end of the sump tube by repeated aspiration whilst withdrawing the tube 10 cm at a time. A new Salem sump tube was used on each occasion. The volume of gastric juice obtained was measured and the pH determined by a Corning 113 pH meter and microelectrode. The generally accepted values for intragastric pH and volume of $\geq 2.5$ and $< 25$ ml respectively were employed as the definition of successful treatment.

Blood samples were collected before and 7 days after omeprazole administration for full blood count and biochemical profile. Further blood samples were obtained at delivery for plasma omeprazole estimation, from the umbilical vein and umbilical artery of the infant and also from a maternal vein in the noninfused arm.

All infants were examined at birth by a neonatologist and Apgar scores given at one and 5 minutes. Gastric aspirates were obtained from babies who required stomach emptying and their pH was determined. The general well-being of the infant was assessed daily for 7 days postpartum.

Results are presented as mean values (SD).

## Results

Twenty patients were included in the study and their mean age, weight and period of gestation were 31 (4.3) years, 69.9 (7.4) kg and 38.3 (0.9) weeks respectively. The mean time from omeprazole administration to induction of anaesthesia was 853 minutes, with a range of 765 to 977 minutes. No side effects of omeprazole treatment were reported during the pre-operative period and the induction, maintenance and emergence from anaesthesia were free of incidents which could be related to its use.

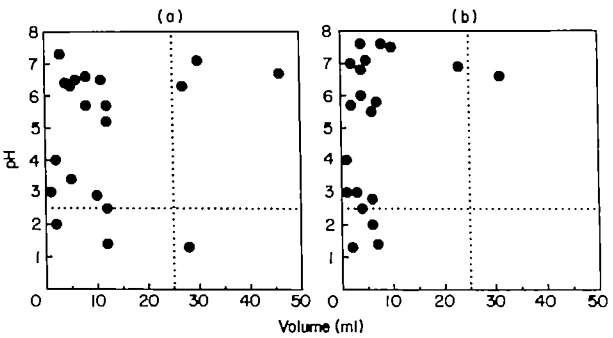


Fig. 2. Intragastric pH and volume in 20 patients admitted for elective Caesarean section after a single 80-mg oral dose of omeprazole; (a) immediately after induction of anaesthesia and (b) before extubation.

Gastric aspirates, immediately after induction and also before reversal of neuromuscular block and extubation were obtained from all patients; their pH and volume is shown in Figure 2. Seventeen of 20 (85%) postinduction and before extubation aspirates had pH values equal to or greater than 2.5, and 16 of the postinduction (80%) and 19 of the pre-extubation volumes (95%) were below 25 ml. The combination of pH $< 2.5$ and volume $> 25$ ml was found in only one patient postinduction and not in any patient at extubation. There was no apparent relationship between the time from omeprazole administration to induction and intragastric pH or volume.

Twenty maternal venous, 17 umbilical arterial and 20 umbilical venous omeprazole plasma levels are shown in

**Table 1.** Omeprazole to general anaesthetic time interval and plasma omeprazole levels for individual patients.

| Case number | Omeprazole to induction time (minutes) | Plasma omeprazole levels (nmol/litre) | | |
|---|---|---|---|---|
| | | Maternal | Umbilical artery | Umbilical vein |
| 1 | 905 | 24 | 0* | 0 |
| 2 | 815 | 44 | x | 0 |
| 3 | 785 | 0 | 0 | 0 |
| 4 | 765 | 122 | 77 | 79 |
| 5 | 829 | 0 | 0 | 0 |
| 6 | 905 | 27 | 0 | 0 |
| 7 | 977 | 105 | 47 | 54 |
| 8 | 880 | 0 | x | 0 |
| 9 | 952 | 0 | 0 | 0 |
| 10 | 855 | 78 | 37 | 33 |
| 11 | 915 | 0 | x | 0 |
| 12 | 810 | 271 | 109 | 0 |
| 13 | 793 | 0 | 0 | 0 |
| 14 | 870 | 0 | 0 | 0 |
| 15 | 780 | 60 | 26 | 0 |
| 16 | 935 | 0 | 21 | 0 |
| 17 | 869 | 0 | 0 | 0 |
| 18 | 769 | 152 | 74 | 80 |
| 19 | 835 | 0 | 0 | 0 |
| 20 | 810 | 0 | 0 | 0 |

*Below minimum detection limit of assay i.e. 20 nmol/litre.
x, No sample obtained.

Table 1. The levels in all samples are low. There was no correlation between maternal plasma levels and the pH of the gastric aspirates. Six of 16 patients with pH $\geq 2.5$ and all patients with pH $< 2.5$ had a concentration lower than the sensitivity of the assay (20 nmol/litre). Sixteen of the umbilical venous samples had omeprazole levels below the measurement limit. There was a similar finding from the umbilical arterial estimates where four of the levels exceeded the corresponding venous levels.

The average Apgar scores at one and 5 minutes were 7.1 (range 4 to 8) and 8.8 (range 7 to 9) respectively. The Apgar 4 score was due to difficulty with delivery of the baby. None of the 20 infants required transfer to the intensive care unit and their 7-day follow-up revealed normal progress. Thirteen gastric aspirates were obtained from babies immediately after delivery and their mean pH was 7.1 (range 6.0 to 8.0).

The pre- and postoperative haemoglobin (g/litre) were 12.4 (0.94) and 12.0 (1.41) respectively. Four of the patients required additional doses of syntocinon to promote uterine contraction and reduce blood loss, but none required blood transfusion. The electrolyte and liver function screen showed no abnormal variations between pre- and post-treatment values.

## Discussion

Omeprazole is absorbed in the small intenstine from the enteric-coated granule formulation used in this study and is activated in the acidic environment of its target cell, the parietal cell.[3] This, combined with its short plasma half-life and rapid elimination from plasma (terminal half-life of 0.5–1.5 hours),[3] results in its specific action within the gastric mucosa. Omeprazole induces a noncompetitive, long-lasting inhibition of gastric acid secretion which, because of the rapid elimination of the drug from plasma, does not correlate with circulating plasma levels. These characteristics suggest that it may be a useful drug to reduce gastric acidity and volume in patients who have general anaesthesia.

Investigations to establish acceptable values for the acidity and volume of gastric contents before general anaesthesia indicate that pH $> 2.5$ and a volume not exceeding 25 ml should be the aim.[5,6] However there are other authorities who believe the critical pH to be 3.0.[7] In a previous study using a similar method, 12 of 14 gastric aspirates from women who received no antacid treatment had a pH below 2.5 and their mean volume was 21 ml (range 5 to 52).[8] It was considered inadvisable to include a no-treatment group in the present investigation because of this finding. However, it has been shown that 80% of the postinduction and pre-extubation aspirates were above the 2.5 pH level and this was some 12–16 hours after omeprazole treatment. Nevertheless, a failure rate of one in five is unacceptable for obstetric anaesthesia. It is noteworthy that some patients with low intragastric pH had aspirate volumes which could be considered safe, but the reliability of the method of determining gastric content volume used here may have resulted in an underestimate, and a dye dilution technique might have produced a more accurate result.[9]

After therapeutic doses of omeprazole, the plasma concentration ranges between 0.19 and 19.4 μmol/litre[10] and levels within this range occurred only once in the maternal plasma estimations, and concentrations below the sensitivity of the assay were frequent. This is consistent with its rapid elimination from plasma. Thus, lack of correlation between the antisecretory effect and plasma concentration in the present study is not a surprising finding.

Omeprazole (molecular weight 345.92) is an ampholyte (pK 3.97 and 8.8) and is 95% bound mainly to albumin and alpha acid glycoprotein. Animal studies suggest that placental transfer does occur.[3,11] The findings here are not inconsistent with animal studies which suggest that maternal plasma levels are the main determinant of fetal levels,[11] since appreciable fetal plasma concentrations were only observed from women with the higher plasma concentrations (Table 1). The pH of the gastric contents of the babies at birth were close to neutrality, which is a normal finding,[12] and further aspirates taken later would be needed to ascertain if acid secretion was suppressed by transferred drug.

This study has shown that omeprazole produces prolonged reduction of acid secretion in the majority of women awaiting elective Caesarean delivery. Its consistency in producing acceptable gastric pH and volume 12 to 16 hours after dose administration was not acceptable. This may have been due to reduced bioavailability in some patients or perhaps to metabolism and excretion with termination of effect on the parietal cell. Presumably its use will also be associated with the delayed onset of action seen with $H_2$ receptor blocker therapy, due to the time required for emptying of existing gastric acid and that necessary to achieve a therapeutic level of the drug. Further study, especially with regard to onset time, peak effect and duration of action are required. Omeprazole gives hope of a single anti-acid therapy for labours up to 12 hours' duration.

## Acknowledgment

This study was supported by a grant from the Astra Clinical Research Unit, Edinburgh. We thank the medical and nursing staff of the Jubilee Maternity and the Ulster Hospital for their help and cooperation.

## References

1. Mendelson CL. The aspiration of stomach contents into the lungs during obstetric anaesthesia. *American Journal of Obstetrics and Gynecology* 1946; **52:** 191–204.
2. Turnbull AC, Tindall VR, Robson G, Dawson IMP, Cloake EP, Ashley JSA. *Report on confidential enquiries into maternal deaths in England and Wales 1979–1981.* London: HMSO: 1986.
3. Clissold SP, Campoli-Richards DM. Omeprazole, A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in peptic ulcer disease and Zollinger–Ellison syndrome. *Drugs* 1986; **32:** 15–47.
4. Howden CW, Forrest JAH, Reid JL. Effects of single and repeated doses of omeprazole on gastric acid and pepsin secretion in man. *Gut* 1984; **25:** 707–10.
5. Roberts RB, Shirley MA. Reducing the risk of acid aspiration during cesarean section. *Anesthesia and Analgesia* 1974; **53:** 859–68.
6. Teabeaut JR. Aspiration of gastric contents: an experimental study. *American Journal of Pathology* 1952; **28:** 51–67.
7. Crawford JS. Cimetidine in elective Caesarean section. *Anaesthesia* 1981; **36:** 641–2.
8. Howe JP, Moore J, McCaughey W, Dundee JW. Effect of cimetidine in reducing intragastric acidity in patients

*Anaesthesia*, 1989, Volume 44, pages 563–566

# Gastric emptying after head injury

I. POWER, J C. EASTON, J. G. TODD AND W. S. NIMMO

## Summary

*Gastric emptying was measured in patients after head injury and compared with that of healthy volunteers using the rate of paracetamol absorption as an indicator of gastric emptying rate. There was a trend towards slower gastric emptying in the head injured patients, but the differences were not statistically significant.*

## Key words

*Trauma*; head injury.
*Gastrointestinal tract*; stomach.

It is a widely held belief that head injury delays gastric emptying.[1] There are important implications for the management of head injured patients if this is so. These include the risk of inhalation of gastric contents (especially during the induction of anaesthesia), delayed absorption of drugs given orally or by nasogastric tube and problems which may occur when attempts are made to start enteral nutrition.

Paracetamol may be used as a model drug for gastric emptying studies.[2,3] Its rate of absorption after oral administration is an indirect measure of the rate of gastric emptying because it is not absorbed to any extent from the stomach but is absorbed rapidly from the small intestine.[4,5] We have used this method to measure the rate of gastric emptying in patients after head injury and compared it with that of healthy volunteers.

## Methods

### *Patients*

Seventeen severely head injured patients [Glasgow Coma Scale (GCS) range 3–10][6] were studied within 54 hours of injury (mean 24.1, range 6–54 hours). Patients with multiple injuries or intra-abdominal trauma were not studied. Approval for the study was obtained from the ethics committee of the Institute of Neurological Sciences, Glasgow. Informed consent was obtained from the relatives of the patients.

The time from the injury to the beginning of the study and any opioids given, and the interval from their administration to the beginning of the study were noted.

A nasogastric tube was inserted, aspirated, and 50 ml of Panadol syrup (1.2 g paracetamol) was instilled in each patient, followed by 20 ml of water. Blood samples (10 ml) were taken at 0, 15, 30, 60, 90, 180, and 300 minutes.

### *Control group*

Nine healthy volunteers (seven males) aged 25–32 (mean 27.4) years formed the control group. Each subject swallowed 1.2 g of paracetamol syrup followed by 20 ml of water after an overnight fast. No food, fluid, or tobacco[7] was allowed during the study and the volunteers remained supine for the first 90 minutes.[8] Blood samples were taken at 0, 15, 30, 60, 90, and 180 minutes. Plasma paracetamol concentrations were measured by high performance liquid chromatography.[9]

### *Data analysis*

Data are displayed as individual values and mean (SD). The area under the concentration time curve at 90 minutes (AUC) was calculated using the trapezoid method. Statistical analysis was by two-tailed Student's *t*-test. Confidence limits (95%) for any differences were calculated. $p < 0.05$ was considered statistically significant.

## Results

Patient details, diagnosis, GCS, highest recorded intracranial pressure, operative procedure and eventual outcome[10] were recorded (Tables 1 and 2). The patients

---

I. Power, BSc, FFARCS, Lecturer, University Department of Anaesthetics, Royal Infirmary, Edinburgh, J.C. Easton, FFARCS, J.G. Todd, FFARCS, Consultant Anaesthetists, Institute of Neurosurgery, Glasgow, W.S. Nimmo, BSc, MD, FRCP, FFARCS, University Department of Anaesthetics, Sheffield.

Accepted 6 December 1988.

0003–2409/89/070563+04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Patient data.

| Patient (sex) | Age (years) | Diagnosis | GCS | ICP (mmHg) | Operation | Outcome |
|---|---|---|---|---|---|---|
| 1 (M) | 42 | SDH | 7 | 14 | Cran | md |
| 2 (M) | 44 | EDH | 7 | 21 | Cran | sd |
| 3 (M) | 45 | SDH | 4 | High | Cran | dead |
| 4 (F) | 41 | DHI | 7 | — | None | md |
| 5 (M) | 61 | SDH | 7 | 16 | Burr | good |
| 6 (M) | 17 | DHI | 7 | — | None | md |
| 7 (M) | 50 | SDH | 3 | High | Cran | dead |
| 8 (M) | 60 | SDH | 5 | 50 | Cran | dead |
| 9 (M) | 18 | DHI | 6 | — | None | good |
| 10 (M) | 59 | SDH | 10 | 15 | Cran | good |
| 11 (M) | 20 | ICH | 7 | — | None | good |
| 12 (M) | 29 | DHI | 4 | 12 | Burr | md |
| 13 (M) | 74 | SDH | 4 | — | Cran | dead |
| 14 (M) | 46 | DHI | 7 | — | None | good |
| 15 (M) | 52 | SDH | 5 | 10 | None | sd |
| 16 (M) | 24 | DHI | 7 | — | None | md |
| 17 (F) | 55 | SDH | 5 | 10 | Cran | sd |
| Mean | 43.4 | | | | | |
| SD | 16.3 | | | | | |

SDH, subdural haematoma; EDH, extradural haematoma; DHI, diffuse head injury; ICH, intracerebral haematoma; ICP, intracranial pressure; GCS, Glasgow Coma Scale; Cran, craniotomy; burr, burr hole; md, moderate disability; sd, severe disability.

were significantly older [mean age 43.4 (16.3) years] than the control group [mean age 27.4 (3.8) years].

Plasma paracetamol concentrations are shown in Tables 3 and 4 and Figure 1. There were no significant differences at any time. However, significance was almost reached at 60 and 90 minutes with p values of 0.16 and 0.07 respectively. The 95% confidence intervals for the difference between the control and patient groups were −1.5 to 8.7 μg/ml and −0.9 to 7.7 μg/ml at 60 and 90 minutes respectively.

The AUC did not differ significantly between the patients and the controls (Table 5).

The mean time to peak paracetamol concentration was 122 minutes for the patient group, and 77 minutes for the control group (Table 6). The 95% confidence interval for this difference of 45 minutes was from −9 to +99 minutes (p = 0.1).

**Table 2.** Patient data (continued).

| Patient | Injury study (hours) | Opioid | Opioid study (hours) |
|---|---|---|---|
| 1 | 30 | Papaveretum | 19 |
| 2 | 11 | Fentanyl | 8 |
| 3 | 23 | None | — |
| 4 | 22 | Codeine | 5 |
| 5 | 48 | Fentanyl | 14 |
| 6 | 18 | None | — |
| 7 | 18 | Morphine | 11 |
| 8 | 42 | None | — |
| 9 | 54 | None | — |
| 10 | 15 | Fentanyl | 7 |
| 11 | 44 | None | — |
| 12 | 11 | Fentanyl | 9 |
| 13 | 22 | None | — |
| 14 | 6 | None | — |
| 15 | 19 | None | — |
| 16 | 14 | None | — |
| 17 | 13 | None | — |
| Mean | 24.1 | | |

**Table 3.** Patient group—plasma paracetamol μg/ml, sampling time in minutes.

| Patient | 15 | 30 | 60 | 90 | 180 |
|---|---|---|---|---|---|
| 1 | 3.3 | 3.3 | 6.0 | 12.7 | 8.9 |
| 2 | 0.9 | 3.3 | 5.2 | 6.3 | 7.8 |
| 3 | 0.4 | 0.4 | 0.4 | 0.9 | 1.1 |
| 4 | 6.7 | 20.5 | 22.1 | 16.6 | 11.5 |
| 5 | 10.7 | 17.9 | 15.1 | 13.9 | 8.4 |
| 6 | 5.7 | 6.4 | 8.4 | 8.2 | 8.6 |
| 7 | 0.5 | 0.5 | 0.6 | 1.0 | 1.7 |
| 8 | 1.1 | 6.5 | 3.6 | 3.3 | 13.3 |
| 9 | 0 | 2.2 | 12.6 | 16.3 | 11.5 |
| 10 | 0 | 6.0 | 12.4 | 11.2 | 4.4 |
| 11 | 13.5 | 20.5 | 14.6 | 13.1 | 11.6 |
| 12 | 2.7 | 7.7 | 13.5 | 15.1 | 7.9 |
| 13 | 3.9 | 3.7 | 3.7 | 0 | 9.7 |
| 14 | 0 | 0 | 0 | 0 | 6.7 |
| 15 | 1.1 | 1.1 | 4.4 | 5.1 | — |
| 16 | 6.3 | 11.8 | 15.5 | 11.8 | 6.6 |
| 17 | 11.3 | 15.5 | 15.8 | 14.3 | 9.6 |
| Mean | 4.0 | 7.5 | 9.1 | 8.8 | 8.1 |
| SD | 4.4 | 7.1 | 6.6 | 6.1 | 3.9 |
| p(*) | 0.93 | 0.95 | 0.16 | 0.07 | 0.6 |

*Compared with controls (Student's *t*-test).

**Table 4.** Control group—plasma paracetamol μg/ml.

| Patient | 15 | 30 | 60 | 90 | 180 |
|---|---|---|---|---|---|
| 1 | 3.7 | 14.7 | 13.9 | 13.9 | 9 |
| 2 | 6.5 | 13.1 | 17.3 | 13.3 | 8.3 |
| 3 | 1.0 | 0.8 | 2.0 | 10.2 | 13.2 |
| 4 | 3.1 | 5.7 | 10.7 | 12.1 | 9.2 |
| 5 | 0 | 4.7 | 17.7 | 12.6 | 10.9 |
| 6 | 0.9 | 3.5 | 13.3 | 11.1 | 5.2 |
| 7 | 5.5 | 11.9 | 13.8 | 15.0 | 9.5 |
| 8 | 0 | 1.7 | 11.8 | 8.7 | 5.8 |
| 9 | 16.9 | 13.1 | 13.6 | 12.7 | 8.5 |
| Mean | 4.2 | 7.7 | 12.7 | 12.2 | 8.8 |
| SD | 5.3 | 5.5 | 4.6 | 1.9 | 2.4 |

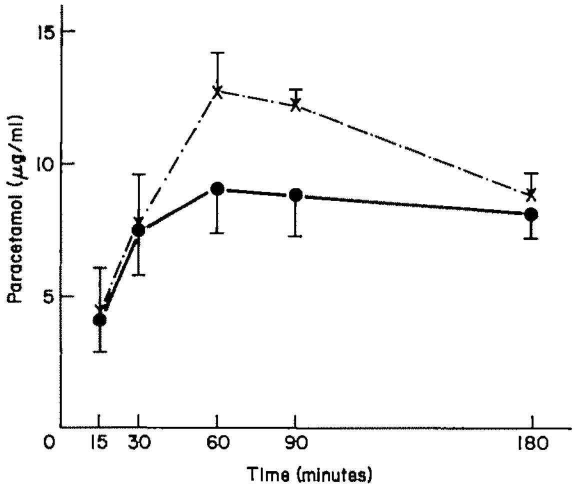


**Fig. 1.** The mean (SE) plasma paracetamol concentrations of the patient and control groups. —·—, controls; —, patients.

## Discussion

Paracetamol absorption and hence gastric emptying did not differ significantly from normal in the control group. The mean plasma paracetamol concentrations at each time were very similar to those reported in a previous study using the same dose and preparation of paracetamol.[3] The patients were older than the control group, but previous studies on the effect of age on drug absorption have demonstrated that after oral administration absorption was not altered appreciably.[11]

The absorption of paracetamol varied widely in the patient group (Table 3). Certain subjects had very slow absorption (numbers 3, 7, 13, 14), and all but one of these four patients (number 14) had a GCS of less than 5 and died of their head injury (Table 1). Other subjects in the head injured group had rapid paracetamol absorption, and most of these patients survived. This study was not large enough to correlate the variability in paracetamol absorption with the severity of head injury, intracranial pressure, or time from ictus.

**Table 5.** $AUC_{0\text{–}90}$ (μg minute/ml).

| | Patients | Controls |
|---|---|---|
| | 494 | 1012 |
| | 338 | 1111 |
| | 40 | 246 |
| | 1472 | 677 |
| | 1224 | 826 |
| | 604 | 658 |
| | 52 | 989 |
| | 320 | 523 |
| | 672 | 1147 |
| | 675 | |
| | 1298 | |
| | 845 | |
| | 252 | |
| | 0 | |
| | 250 | |
| | 1002 | |
| | 1207 | |
| Mean | 632 | 799 |
| SD | 474 | 299 |
| p | 0.65 | |

**Table 6.** Time to peak paracetamol concentration (minutes).

| | Patients | Controls |
|---|---|---|
| | 90 | 30 |
| | 180 | 60 |
| | 180 | 180 |
| | 60 | 90 |
| | 30 | 60 |
| | 180 | 60 |
| | 180 | 90 |
| | 180 | 60 |
| | 90 | 60 |
| | 60 | |
| | 30 | |
| | 90 | |
| | 180 | |
| | 300 | |
| | 90 | |
| Mean | 122 | 77 |
| SD | 73 | 43 |
| p | 0.1 | |

A significant difference was approached, but not attained at 60 and 90 minutes when the mean plasma paracetamol concentrations for the head injured and control groups were compared using Student's *t*-test. However the confidence intervals for the differences in paracetamol concentrations between the groups at these times are strongly suggestive of a reduction of paracetamol absorption in the head injured group. In addition the mean paracetamol concentration was lower in the head injured group at each observation time (Fig. 1).

Comparison of the time to peak paracetamol concentration revealed a trend towards a delay in the head injured group in a similar manner, as shown by the confidence intervals. However, this did not reach statistical significance.

This study may indicate clinically important delayed gastric emptying in head injured patients which did not achieve statistical significance upon hypothesis testing because of the small number of subjects involved. The problems of reporting such a study have been discussed recently and the suggestion made that simple hypothesis testing may not be the best way to consider such data.[12] Instead it may be preferable to analyse and display the observed difference between experimental groups by the calculation of confidence intervals. The confidence intervals in this study for paracetamol concentration (at 60 and 90 minutes) and for the time to peak paracetamol concentration are indicative of impaired gastric emptying in the patient group.

The results of this study would also be consistent with the hypothesis that a small subgroup of the patients had markedly impaired gastric emptying. Those patients with the most obvious delay in gastric emptying tended to have very severe injury, with Glasgow Coma Scores of less than 5. Future investigation of this problem should be focused on these patients.

## Acknowledgment

We are grateful to the Scottish Hospital Endowments Research Trust for financial support.

## References

1. Frost EAM. The physiopathology of respiration in neurosurgical patients. *Journal of Neurosurgery* 1979; **50:** 699–714.
2. Nimmo WS, Wilson J, Prescott LF. Narcotic analgesics and delayed gastric emptying during labour. *Lancet* 1975; **I:** 890–3.
3. Goldstraw P, Bach P. Gastric emptying after oesophagectomy as assessed by plasma paracetamol concentrations. *Thorax* 1981; **36:** 493–6.
4. Heading RC, Nimmo J, Prescott LF, Tothill P. The dependence of paracetamol absorption on the rate of gastric emptying. *British Journal of Pharmacology* 1973; **47:** 415–21.
5. Clements JA, Heading RC, Nimmo WS, Prescott LF. Kinetics of acetaminophen absorption and gastric emptying in man. *Clinical Pharmacology and Therapeutics* 1978; **24:** 420–31.
6. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974; **2:** 81–4.
7. Grimes DS, Goddard J. Effect of cigarette smoking on gastric emptying. *British Medical Journal* 1978; **2:** 460–1.
8. Nimmo WS, Prescott LF. The influence of posture on paracetamol absorption. *British Journal of Clinical Pharmacology* 1978; **5:** 348–9.
9. Howie D, Adriaenssens PI, Prescott LF. Paracetamol metabolism following overdosage: application of high performance liquid chromatography. *Journal of Pharmacy and Pharmacology* 1977; **29:** 235–7.
10. Jennett B, Bond M. Assessment of outcome after severe brain damage. A practical scale *Lancet* 1975; **1:** 480–4.
11. Stevenson IH, Salem SAM, O'Malley K, Cusack B, Kelly GJ. Age and drug absorption. In: Prescott LF, Nimmo WS, eds. *Drug absorption (Proceedings of the Edinburgh International Conference)*. New York: Adis Press, 1979: 259.
12. Gardner MJ, Altman DG. Confidence intervals rather than P values: estimation rather than hypothesis testing. *British Medical Journal* 1986; **292:** 746–50.

*Anaesthesia*, 1989, Volume 44, pages 567–570

# Atracurium infusion during paediatric craniofacial surgery

## Closed loop control of neuromuscular block

C. M. WAIT AND V. A. GOAT

### Summary

*A simple feedback control system was used to administer atracurium to 10 infants aged between 5 and 36 months during craniofacial reconstruction. The purpose of the study was to establish whether the system, previously evaluated only in adults, would be effective in paediatric patients. The individuals studied underwent long procedures with substantial blood loss and the potential for thermal and electrolyte disturbances. The system maintained the level of neuromuscular block successfully between 88 and 100% in all patients and between 90 and 100% in nine patients. The mean duration of feedback control was 179 (range 111–440) minutes. The mean (SD) dose of atracurium required was 0.40 (0.12) mg/kg/hour. The mean (SD) recovery time to a train-of-four ratio of 0.75 was 24.8 (9.9) minutes.*

**Key words**

*Neuromuscular relaxants*; atracurium.
*Surgery*; craniofacial.

The correction of congenital abnormalities of the skull, face and orbits may require several hours of surgery and anaesthesia. Blood loss may be considerable during these procedures; in small children, up to four times the blood volume may be replaced during surgery.[1] Large transfusions and potential disturbances of fluid, electrolyte and thermal balance dictate that neuromuscular blocking drugs be used with particular care because dose requirements may vary unpredictably during the procedure. This could result in underdosage and inadequate relaxation, or overdosage with prolonged blockade and difficulty in reversal. Inadequate relaxation, with the risk that the patient may cough or strain during the procedure, is particularly undesirable for intracranial operations. It is desirable that reversal from neuromuscular block should be achieved rapidly at the end of the procedure to allow extubation and early neurological assessment.

A feedback controlled system should be able to maintain a constant level of neuromuscular block in the face of a wide range of infusion requirements. The purpose of this study was to determine whether a feedback system, evaluated previously in adults,[2] could cope with the extreme problems posed by this type of surgery in infants.

## Methods

The project was discussed with the local ethics committee and the informed consent of the infants' parents was obtained verbally.

### *Selection of patients*

Ten consecutive infants and children under the age of 3 years were studied. All were scheduled for elective correction of a congenital craniofacial abnormality.

### *Anaesthetic management*

Children who weighed less than 10 kg were premedicated with atropine 0.1–0.2 mg intramuscularly. Heavier children received oral diazepam 0.2 mg/kg in addition to atropine. Anaesthesia was induced in all cases with halothane in 70% nitrous oxide and oxygen. Tracheal intubation was facilitated by administration of suxamethonium 1.5 mg/kg. The volatile agent was then discontinued and anaesthesia was maintained with nitrous oxide in oxygen and fentanyl 10–20 μg/kg with further increments of fentanyl as indicated clinically. A bolus dose of thiopentone 5 mg/kg was administered and followed by an infusion of thiopentone at a rate of 2 mg/kg/hour for the duration of the procedure. The thiopentone infusion was used to help to reduce intracranial pressure and to minimise the possibility of awareness. Two peripheral venous lines were sited, for crystalloid fluid and blood respectively. The radial or brachial artery was cannulated for arterial pressure monitoring and blood gas estimations. Ventilation was adjusted to maintain the $Pa\text{CO}_2$ between 3.5 and 4.0 kPa. Rectal and peripheral skin temperatures were monitored continuously. Heat loss was minimised by induction of anaesthesia under an overhead

C.M. Wait, BM, BCh, FFARCS, Senior Registrar, V.A. Goat, MB, ChB, FFARCS, Consultant, Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford OX2 6HE.

Accepted 1 February 1989.

0003–2409/89/070567+04 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Details of patients.

| Patient | Age (months) | Weight (kg) | Diagnosis |
|---|---|---|---|
| 1 | 7 | 10.6 | Pfeiffer's syndrome |
| 2 | 30 | 7.0 | Multiple anomalies |
| 3 | 28 | 4.0 | Crouzon's syndrome |
| 4 | 6 | 6.2 | Pfeiffer's syndrome |
| 5 | 36 | 10.0 | Crouzon's syndrome |
| 6 | 28 | 13.8 | Plagiocephaly |
| 7 | 6 | 7.2 | Brachycephaly |
| 8 | 7 | 6.0 | Plagiocephaly |
| 9 | 5 | 7.8 | Plagiocephaly |
| 10 | 5 | 7.0 | Crouzon's syndrome |
|  | Median 7 | Mean 8.0 (SD) 2.8 |  |

heater, humidification of gases and by warming fluids. The theatre temperature was maintained at 28°C.

*Feedback control system*

The system and its evaluation in adult patients have been described previously.[2] Neuromuscular transmission was monitored by a Datex Relaxograph (Vickers Medical). The Relaxograph is a microprocessor-controlled electromyographic analyser which generates supramaximal 'train-of-four' stimuli at 20-second intervals and displays a value for both T1 (the first twitch of the train-of-four) and for TR (the train-of-four ratio).[3] The 'T1 High Alarm' of the Relaxograph is used to trigger a relay which in turn switches on a syringe pump that contains atracurium. Recovery of neuromuscular transmission above the level set on the T1 alarm results in infusion of atracurium until the level of block again decreases below the selected level. The result is that the degree of neuromuscular block oscillates around the selected level until the feedback loop is interrupted, when spontaneous recovery starts. Profound relaxation is desirable for these combined plastic and neurosurgical procedures. Consequently, the T1 alarm was set at 4% in the expectation that neuromuscular block could be maintained at less than 10% of the control Tl.

The ulnar nerve was stimulated in this study at the elbow via standard pregelled electrocardiograph electrodes. The recording electrodes were placed over the hypothenar eminence after the skin had been degreased carefully with alcohol to ensure good electrode contact and adhesion. The arm was immobilised and wrapped in cotton wool to reduce limb heat loss. The patient and limb were covered with a metallised heat-reflecting blanket.

A period of 30 minutes was allowed to ensure recovery from the effects of halothane and suxamethonium. The Relaxograph was then calibrated to establish a supramaximal stimulus and to define the 100% value for T1 in the unparalysed state. Atracurium 0.5 mg/kg was administered as a bolus dose and the feedback system was switched on when the train-of-four response was abolished. The syringe pump was set to deliver atracurium at a fixed rate of 1.5 mg/kg/hour. Atracurium was diluted to a concentration of 1 mg/ml in 0.9% w/v saline, and entered the crystalloid infusion via a remote injection port at the venous cannula. All other drugs were given into the colloid line.

The feedback system was inactivated towards the end of surgery to permit recovery from neuromuscular block. Neuromuscular block was antagonised in four patients when T1 had recovered to 25% of control. The remaining six patients were reversed when T1 had recovered to 75%. All patients received 1 ml/6 kg of a mixture of neostigmine 2.5 mg and atropine 0.6 mg diluted to 5 ml. The trachea was extubated when the infant was breathing adequately and moving all four limbs vigorously. Neuromuscular data from the Relaxograph were collected and stored by a microcomputer to facilitate subsequent analysis.

## Results

Details of the patients are summarised in Table 1. The median age was 7 (range 5–36) months and the mean weight was 8.0 (range 4–13.8) kg. There was no history of neuromuscular disease and no patient was receiving any medication known to interact with muscle relaxants.

Neuromuscular data are summarised in Tables 2 and 3. The mean time from the loading dose of atracurium to 4% recovery of T1 (and the initial cut-in of the feedback system) was 30.1 (range 20–40) minutes. The mean duration of feedback control was 179 (range 111–440) minutes. The level of neuromuscular block was maintained by the control system at between 90 and 100% in all but one patient (patient 7). The maximum amplitude of oscillation about the chosen 96% level of block is shown for

Table 2. Neuromuscular data.

| Patient | Time to recovery to 4% after loading dose (minutes) | Duration of feedback control (minutes) | Maximum range of block (% of T1 control) | Mean infusion rate (mg/kg/hour) |
|---|---|---|---|---|
| 1 | 29 | 115 | 92–100 | 0.42 |
| 2 | 32 | 185 | 90–100 | 0.32 |
| 3 | 20 | 190 | 94–97 | 0.39 |
| 4 | 27 | 111 | 94–100 | 0.61 |
| 5 | 25 | 440 | 94–97 | 0.61 |
| 6 | 30 | 150 | 93–100 | 0.36 |
| 7 | 40 | 150 | 88–100 | 0.30 |
| 8 | 33 | 113 | 94–100 | 0.35 |
| 9 | 33 | 165 | 93–100 | 0.37 |
| 10 | 32 | 170 | 94–100 | 0.25 |
| Mean | 30.1 | 179 |  | 0.40 |
| (SD) | 5.1 |  |  | 0.12 |

**Table 3.** Neuromuscular recovery data.

| Patient | Spontaneous recovery time (minutes) | | Time from loop off to TR 0.75 (minutes) |
|---|---|---|---|
| | 5–25% T1 | 25–75% T1* | |
| 1 | 6 | 9 | 19 |
| 2 | 12 | 11 | 32 |
| 3 | 7 | 6 | 22 |
| 4 | 10 | 15 | 29 |
| 5 | 23 | 24 | 51 |
| 6 | 6 | 7 | 17 |
| 7 | 8 | – | 20 |
| 8 | 8 | – | 21 |
| 9 | 9 | – | 17 |
| 10 | 11 | – | 20 |
| Mean | 10 | 12.0 | 24.8 |
| (SD) | 5.0 | 6.7 | 9.9 |

*Patients 1–6: reversal given when T1 = 75%; patients 7–10: reversal given when T1 = 25%.
TR, train-of-four ratio.

each patient in Table 2. A representative Relaxograph printout is shown in Figure 1.

Relaxation was clinically satisfactory in all infants although in patient 7 the level of block recovered to a T1 of 12% before it was noticed that the crystalloid infusion bag was empty; this had resulted in discontinuation of atracurium administration. The mean (SD) dose requirement of atracurium during feedback control was 0.40 (0.12) mg/kg/hour. There appeared to be no obvious relationship between infusion requirements and peroperative blood replacement, which ranged from 59 to 250% of estimated blood volume.

There was no difficulty with prolonged block or inadequate reversal. The times for recovery of T1 from 5–25% and from 25–75% of T1 at full recovery are shown in Table 3. Full recovery of T1 was to between 95 and 105% of control in seven patients. Apparent full recovery of T1 occurred in the other three at between 88 and 110% of the original control value. The 25 and 75% recovery points for T1 were obtained by extrapolation from the value of T1 at full recovery. The mean (SD) time from inactivation of the feedback system to recovery of TR of 0.75 was 24.8 (9.9) minutes. Administration of neostigmine when T1 had recovered to 25% of control ($n = 4$) did not result in a significantly shorter recovery time (Mann–Whitney *U* test) than later reversal at T1 = 75% ($n = 6$).

## Discussion

A number of feedback systems for the automated administration of relaxants have been reported. These include simple 'on-off' systems which repeatedly activate a fixed-rate infusion,[2,4] and more complex proportional control systems which adjust the rate of infusion in an attempt to achieve and maintain the desired setpoint.[5,6] This paper describes further experience with one of the simplest systems. It has proved to be able to achieve and maintain a stable level of neuromuscular block with atracurium in infants. More refined systems are able to minimise oscillation around the setpoint;[6] nevertheless, this system maintained the level of block within a range that is more than adequate for clinical purposes. The desired level of block was achieved in a mean time of 30.1 (range 20–40) minutes after the loading dose of atracurium.

The reliable performance of a feedback control system depends crucially on the accuracy of monitoring. The use of the evoked compound electromyogram has been shown by some workers to underestimate the degree of neuromuscular block.[7] These authors compared the Datex NMT221 Neuromuscular Transmission Monitor with isometric twitch recording, using tubocurarine. Other investigators, who used atracurium, found a better correlation between the Relaxograph and mechanically transduced measurements.[3] Positioning of the Relaxograph electrodes can be difficult in infants. It was found during preliminary studies that stimulation of the ulnar nerve at the wrist whilst recording over the hypothenar eminence led to an unacceptably high stimulus artefact; this was minimised by stimulation of the ulnar nerve at the elbow. It is important to ensure that movement of the arm is prevented because this can alter the relationship between the stimulating electrodes and the underlying nerve, and result in a change of threshold for supramaximal stimulation.

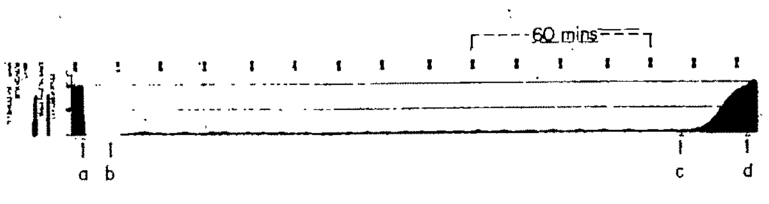


**Fig. 1.** Relaxograph printout during feedback control of neuromuscular block in a 28-month, 4-kg female who underwent craniofacial reconstruction for Crouzon's syndrome. a, loading dose of atracurium (0.5 mg/kg); b, feedback system activated; c, feedback control discontinued; d, neostigmine.

The importance of maintaining limb temperature above 32°C during neuromuscular monitoring has been highlighted recently.[8] In this study rectal temperature was maintained above 35.5°C in all patients and the core–peripheral temperature gradient never exceeded 1.8°C.

The mean dose requirement for atracurium (0.40 mg/kg/hour) and the relatively wide range (SD 0.12) are similar to values obtained in adults during balanced anaesthesia.[9]

The level of block selected for these major neurosurgical procedures was profound, but the rate of recovery after interruption of the feedback loop was very satisfactory. However, the range of recovery times was wide. This interpatient variation demonstrates the need for careful clinical assessment and monitoring to confirm that reversal is adequate.

In conclusion, this simple feedback control system provided clinically satisfactory control of neuromuscular block during long and haemorrhagic procedures in normothermic infants. Both over- and underdosage were avoided and reliable reversal was achieved easily in all cases.

## Acknowledgments

We are grateful to our surgical colleagues whose patients we studied, to the Wellcome Foundation who provided the Relaxograph, and to Dr C.E. Blogg for his helpful suggestions during the preparation of the manuscript.

## References

1. Uppington J, Goat VA. Anaesthesia for major craniofacial surgery: a report of 23 cases in children under four years of age. *Annals of the Royal College of Surgeons of England* 1987; **69:** 175–8.
2. Wait CM, Goat VA, Blogg CE. Feedback control of neuromuscular blockade. A simple system for infusion of atracurium. *Anaesthesia* 1987; **42:** 1212–7.
3. Carter JA, Arnold R, Yate PM, Flynn PJ. Assessment of the Datex Relaxograph during anaesthesia and atracurium-induced neuromuscular blockade. *British Journal of Anaesthesia* 1986; **58:** 1447–52.
4. De Vries JW, Ros HH, Booij LHDJ. Infusion of vecuronium controlled by a closed-loop system. *British Journal of Anaesthesia* 1986; **58:** 1100–3.
5. Asbury AJ, Linkens DA. Clinical automatic control of neuromuscular blockade. *Anaesthesia* 1986; **41:** 316–20.
6. Webster NR, Cohen AT. Closed-loop administration of atracurium. Steady-state neuromuscular blockade during surgery using a computer closed-loop atracurium infusion. *Anaesthesia* 1987; **42:** 1085–91.
7. Eisenkraft JB, Pirak L, Thys DM. Monitoring neuromuscular blockade: emg vs twitch tension. *Anesthesia and Analgesia* 1986; **65:** S47.
8. Thornberry EA, Mazumdar B. The effect of changes in arm temperature on neuromuscular monitoring in the presence of atracurium blockade. *Anaesthesia* 1988; **43:** 447–9.
9. Savarese JJ, Gargarian M, Scott RPF, Embree PB, Ali HH, Basta SJ, Sunder N, Weakly JN, Batson AG. Efficacy of atracurium as a continuous infusion. *British Journal of Anaesthesia* 1986; **58:** 55S.

*Anaesthesia*, 1989, Volume 44, pages 571–573

# Postspinal headache in young and elderly patients

## Two randomised, double-blind studies that compare 20- and 25-gauge needles

B. S. RASMUSSEN, L. BLOM, P. HANSEN AND S. S. MIKKELSEN

### Summary

*In two randomised, double-blind studies of elderly patients with a mean age of 68.9 (range 21–88) years and young patients, mean age 29.4 (range 20–40) years, the effect of needle size on the incidence of postspinal headache was compared. The two needle groups, 20- and 25-gauge, were comparable in both studies with regard to number, sex, age and type of surgery. The incidence of postspinal headache in young patients was 27.6% when a 20-gauge needle was used and 12.6% with a 25-gauge needle. There was no significant difference in either the incidence of headache in the elderly patients (10.8% and 7.8%, respectively) or between the sexes. It is concluded that it does not matter if a 20- or a 25-gauge needle is used for spinal analgesia in elderly patients with regard to postspinal headache, but if spinal analgesia is indicated in young patients a fine needle is preferred.*

**Key words**

*Anaesthetic techniques, regional*; spinal.
*Complications*; headache.

Headache is a common complication of spinal analgesia and depends on posture. Any attempt to sit or stand elicits a severe and often circumferential headache, which is relieved by lying down. This postspinal headache seems to be related to subdural hypotension attributable to a continued leakage of cerebrospinal fluid (CSF) though the dural hole made by the needle.[1]

The reported incidence varies widely, between 1.2% and 46%.[1-13] It is suggested use of small-diameter needles is followed by a lower incidence of headache and therefore fine-gauge needles are generally recommended. However, only one of these studies was performed in a randomised, double-blind fashion.

The purpose of the present studies was to evaluate the effect of needle size on the incidence of postspinal headache in young and old patients. Both studies were designed as randomised, double-blind trials. Study 1 involved a homogeneous group of patients who were admitted for elective total hip replacement, while study 2 involved a homogeneous group of young patients between the ages of 20 and 40 years, who all were mobilised on the first day after operation.

## Methods

The two studies involved 400 consecutive patients. The inclusion criteria for study 1 was admission for elective total unilateral hip replacement, while for study 2 patients had to be aged between 20 and 40 years and admitted for either elective or acute orthopaedic, lower abdominal or urogenital surgery. Exclusion criteria were any contraindication to local analgesia, migraine or chronic headache and request for general anaesthesia. The patients were randomly allocated in a double blind manner to either a 20-gauge (Mediplast) or a 25-gauge (Vygon) needle group. All patients were visited before operation by one of the authors. The possibility of postspinal headache was not mentioned during this visit and the nurses in the wards were instructed not to inform the patients. The authors as well as the patients were blinded with respect to needle size.

Premedication consisted of diazepam 5–15 mg orally. Spinal anaesthesia was performed by the department anaesthetists, but did not include the authors. The midline approach in the third or fourth lumbar interspace was used with the patient in the lateral recumbent position. Four millilitres of isobaric plain bupivacaine 0.5% was used throughout. The needle was then withdrawn and the patient immediately turned supine. Ephedrine 50 mg was injected intramuscularly in all cases. An intraveneous infusion was established before dural puncture and one litre of saline given during surgery. Peroperatively sedation in the form of phenobarbitone 50–100 mg intravenously was given if required. The patients in study 1 were interviewed by one of the authors on the fourth day after surgery, and they were first fully mobilised on the third postoperative day because of the nature of operation. The patients in study 2 were interviewed the day after and 3 days after the operation. Any patient discharged from the hospital before

---

B.S. Rasmussen, MD, L. Blom, MD, Senior Registrars, P. Hansen, MD, S.S. Mikkelsen, MD, Registrars, Department of Anaesthesia, Central Hospital, DK-7500 Holstebro, Denmark.

Accepted 24 January 1989.

0003–2409/89/070571+03 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

the third day was contacted by telephone. Headache was classified as postspinal or nonposture-dependent.

For statistical evaluation of the data, the Fisher's exact test (two-tailed) and Student's *t*-test were used.

The studies were approved by the local ethics committee.

## Results

Seventeen patients were excluded from study 1 in the pre- and postoperative period. It was impossible to perform the spinal with the prescribed 25-gauge needle in four patients; seven had an incomplete block, of whom five had a supplementary general anaesthetic and two another spinal injection; four had major cardiovascular complications, one had a classical migraine first noticed postoperatively and another needed a further spinal anaesthetic on the second postoperative day because the artificial hip dislocated. Seven patients were excluded in study 2. It was impossible to perform the spinal with a 25-gauge needle in one patient; two needed a supplementary general anaesthetic, one another spinal anaesthetic, while three had a history of migraine first noticed postoperatively.

The two needle groups in each study were comparable with regard to number, age and sex (Table 1), and in study 2 the needle groups were comparable with regard to type of surgical intervention. Orthopaedic surgery was performed in 72 patients in the 20-gauge needle group and in 73 patients in the 25-gauge group in study 2; lower abdominal surgery was performed in seven patients in each needle group and urogenital surgery in 19 and 15 patients, respectively.

The incidence of postspinal and nonposture-dependent headache in the two needle groups in both age groups is shown in Table 2. Seventeen patients in study 1 with a mean age of 68.9 (range 50–82) years developed postspinal headache. There was no significant difference in the incidence between the two needle sizes ($0.60 < p < 0.70$). Thirty-nine patients in study 2, with a mean age of 28.0 (range 20–40) years developed headache. The incidence was significantly higher after use of a 20-gauge needle compared with a 25-gauge. There was no significant difference in either study in the incidence between women and men. The incidence of nonposture-dependent headache was higher in study 1 than in study 2. There was no significant difference in either between the two needle groups. The four interviewers found the same incidence of postspinal headache.

All patients in study 2 were asked which kind of anaesthetic they would prefer for a similar procedure in the future. Spinal analgesia was preferred by 177 (91.7%) and general anaesthesia by 16. Thirteen of the 16 patients who preferred general anaesthesia had a postspinal headache.

**Table 1.** Data of the patients in the two studies.

| | 20-gauge needle group | 25-gauge needle group |
|---|---|---|
| *Study 1* | | |
| Total number | 93 | 90 |
| Male/female | 43/50 | 44/46 |
| Mean age, years (range) | 68.8 (45–88) | 69.1 (21–82) |
| *Study 2* | | |
| Total number | 98 | 95 |
| Male/female | 80/18 | 68/27 |
| Mean age, years (range) | 29.2 (20–40) | 29.7 (20–40) |

## Discussion

The incidence of postspinal headache has been reported between 1.2% and 46.0%.[1–13] The occurrence of headache is usually unpredictable, but three factors do seem to have an influence, namely size of needle and age and sex of patients.

The leakage of CSF and the subsequent headache has been claimed to be effectively diminished by use of fine needles for the lumbar puncture.[1–3,5–7,9,13] However, when these studies are compared, there seems to be a considerable variation in the incidence of postspinal headache for each individual needle size, varying from 1.5% to 46.0% with an 18-gauge,[4,5,8] from 14.0% to 38.0% with a 20-gauge,[1,10] from 3.4% to 36.0% with a 22-gauge,[1,5–7,9,13] and from 1.2% to 37.2% with a 25-gauge needle.[5,6,9,11,12] Recently, a surprisingly low incidence (one in 117 patients) of postspinal headache was found after continuous spinal analgesia using an 18-gauge needle and a 20-gauge catheter.[14] The incidence seems to decrease with age[1,3,11,13] and to be higher in women than in men.[3,6,13] However, in patients under the age of 13 years the incidence has been reported to be very low.[15]

Most of these clinical trials included nonhomogeneous patient groups in either retrospective[1–3] or prospective[4–12] studies. The groups of patients are not comparable with regard to numbers, sex, age and nature of surgical intervention, even in the individual studies. The method of questioning patients also differs. Postspinal headache in some studies was evaluated by the anaesthetist who performed the anaesthetic[5,7,12] and in others a questionnaire was used.[2,3,9,11] Furthermore, some of these studies only involved neurological patients,[4,10] in whom 10 to 12 ml CSF was withdrawn. Only a single previous study was designed as a randomised, double-blind clinical trial that compared the effect of needle size with the incidence of postspinal headache.[13] However, this study involved healthy volunteers, who, in addition to the lumbar puncture, had 20 ml CSF removed, which in itself may influence the incidence of postspinal headache.

The present studies were designed as randomised, double-blind trials and involved a homogeneous group of

**Table 2.** Incidence of postspinal and nonposture-dependent headache in the two needle groups in the two studies.

| | 20-gauge needle group | 25-gauge needle group |
|---|---|---|
| *Study 1* | | |
| Postspinal headache | | |
| Total incidence | 10/93 (10.8%) | 7/90 (7.8%) |
| Male | 3/43 (6.8%) | 1/44 (2.3%) |
| Female | 7/50 (14.0%) | 6/46 (13.0%) |
| Nonposture-dependent | | |
| Total incidence | 15/93 (16.1%) | 13/90 (14.4%) |
| Male | 7/43 (16.3%) | 3/44 (6.8%) |
| Female | 8/50 (16.0%) | 10/46 (21.7%) |
| *Study 2* | | |
| Postspinal headache | | |
| Total incidence | 27/98 (27.6%)* | 12/95 (12.6%)* |
| Male | 23/80 (28.8%)* | 8/68 (11.8%)* |
| Female | 4/18 (22.2%) | 4/27 (14.8%) |
| Nonposture-dependent | | |
| Total incidence | 4/98 (4.1%) | 5/95 (5.2%) |
| Male | 3/80 (3.8%) | 1/68 (1.5%) |
| Female | 1/18 (5.6%) | 4/27 (14.8%) |

*$p < 0.05$.

patients. The two needle groups were equal with regard to numbers, sex and age of patients as well as type of surgery, in both studies. Factors which may influence the incidence of postspinal headache, especially migraine and other causes of chronic headache,[7] resulted in exclusion from the trial. This was not the case in the above mentioned studies. The investigators and all the patients were blinded with respect to needle size and the patients were not informed of the possibility of postspinal headache, since psychogenic factors may influence the incidence.[16,17] All patients were interviewed by one of the authors, who found the same incidence of postspinal headache. A sharp distinction was maintained between the two types of headache, postspinal and nonposture.

All except one patient in study 1 were older than 40 years and no significant difference in the incidence of postspinal headache was found between a 20- and 25-gauge needle (10.8% and 7.8%, respectively). A significantly higher incidence of postspinal headache was found in our young patients when the 20-gauge needle was used (27.6% and 12.6%). This is in accordance with the results of Tourtellotte *et al.*[13] who found an incidence of 36% when they used a 22-gauge needle and 12% with a 26-gauge. However, their study involved healthy volunteers who also had 20 ml CSF removed. Flaatten *et al.*[11,12] by way of comparison found a higher incidence of headache, 37.2% and 24.5%, when they used a 25-gauge needle for spinal analgesia in younger patients (18–58 years). The design of the studies may have influenced the differences compared with our results as discussed above. The main difference is the pre-operative information given to the patients; Flaatten *et al.*[11,12] informed their patients about the possibility of headache, which we did not. This difference may partly explain the different incidences, since a psychogenic factor has been postulated to influence the occurrence of headache.[16,17] This psychogenic factor may also indirectly have influenced the number of patients who preferred a spinal analgesia for a similar procedure in the future. Flaatten *et al.*[12] found that only 68.6% of the patients would prefer spinal analgesia in the future, compared to 91.7% in our study.

The present studies showed a very low incidence (4.7%) of nonposture-dependent headache in young patients and a higher incidence (15.3%) in elderly patients. This contrasts with other studies,[11,12] in which nonposture-dependent headaches were found to be nearly as frequent as postspinal headache. The difference in the incidence between young and elderly patients in the present studies may be due to the variation in types of surgery.

The incidence of postspinal headache in our studies indicates that they are a more pronounced problem in young patients and that the diameter of the needle plays a significant role only in this age group. We found no significant difference in the incidence between the sexes, which contrasts with several other studies in which females have been found to have a higher incidence.

In conclusion, the incidence of postspinal headache in elderly patients is independent of the diameter of the spinal needle. A thicker needle could therefore be used in elderly patients, if technical difficulties were expected by using a small-diameter needle. In contrast, the incidence of postspinal headache in young patients is high, but it can be effectively diminished by using a fine-gauge needle. Therefore, if a spinal analgesia is indicated in young patients a fine needle is preferred.

## References

1. Vandam LD, Dripps RD. Long-term follow-up of patients who received 10 098 spinal anesthetics. Syndrome of decreased intracranial pressure (headache and ocular and auditory difficulties). *Journal of the American Medical Association* 1956; **161:** 586–91.
2. Kortum K, Rossler B, Nolte H. Morbidity following spinal anaesthesia. *Regional-Anaesthesie* 1979; **2:** 5–11.
3. Kortum K, Nolte H, Kenkmann HJ. Sex difference related complication rates after spinal anaesthesia. *Regional-Anaesthesie* 1982; **5:** 1–6.
4. Sciarra D, Carter S. Lumbar puncture headache. *Journal of the American Medical Association* 1952; **148:** 841–2.
5. Meyer-Hamme K, Stratmann D, Watermann WF, Gotte A. Postspinal headache—a clinical problem. *Regional-Anaesthesie* 1979; **2:** 77–80.
6. Driessen A, Mauer W, Fricke M, Kossmann B, Schleinzer W. Prospective studies of the post-spinal headache. *Regional-Anaesthesie* 1980; **3:** 38–41.
7. Kaukinen S, Kaukinen L, Kannisto K, Kataja M. The prevention of headache following spinal anaesthesia. *Annales Chirurgiae et Gynaecologie* 1981; **70:** 107–11.
8. Carbaat PAT, Van Crevel H. Lumbar puncture headache: controlled study on the preventive effect of 24 hours' bed rest. *Lancet* 1981; **II:** 1133–5.
9. Eckstein KL, Rogacev Z, Vicente-Eckstein A, Grahovac Z. Prospective comparative study of postspinal headaches in young patients ( < 51 years). *Regional-Anaesthesie* 1982; **5:** 57–61.
10. Hilton-Jones D, Harrad RA, Gill MV, Warlow CP. Failure of postural manoeuvres to prevent lumbar puncture headache. *Journal of Neurology, Neurosurgery, and Psychiatry* 1982; **45:** 743–6.
11. Flaatten H, Raeder J. Spinal anaesthesia for outpatient surgery. *Anaesthesia* 1985; **40:** 1108–11.
12. Flaatten H, Rodt S, Rosland J, Vamnes J. Postoperative headache in young patients after spinal anaesthesia. *Anaesthesia* 1987; **42:** 202–5.
13. Tourtellotte WW, Henderson WG, Tucker RP, Gilland O, Walker JE, Kokman E. A randomized, double-blind clinical trial comparing the 22 versus 26 gauge needle in the production of the post-lumbar puncture syndrome in normal individuals. *Headache* 1972; **12:** 73–8.
14. Denny N, Masters R, Pearson D, Read J, Sihota M, Selander D. Postural puncture headache after continuous spinal anesthesia. *Anesthesia and Analgesia* 1987; **66:** 791–4.
15. Bolder PM. Postlumbar puncture headache in pediatric oncology patients. *Anesthesiology* 1986; **65:** 696–8.
16. Kaplan G. The psychogenic etiology of headache post lumbar puncture. *Psychosomatic Medicine* 1967; **29:** 376–9.
17. Daniels AM, Sallie R. Headache, lumbar puncture, and expectation. *Lancet* 1981; **I:** 1003.

*Anaesthesia*, 1989, Volume 44, pages 574–577

# Migration of thoracic epidural catheters

## Three methods for evaluation of catheter position in the thoracic epidural space

J. MOURISSE, M. J. M. GIELEN, M. A. W. M. HASENBOS AND F. M. J. HEYSTRATEN

## Summary

*Migration of thoracic epidural catheters was evaluated in 25 patients by three methods either after placement of the catheter or immediately after surgery. The first method was the determination of the depth of the catheter from the skin, the second the determination of the level of sensory blockade which resulted from a test dose of a local anesthetic agent, while the third consisted of radiological visualisation of the catheter tip in the epidural space with radiopaque dye. The evaluations were repeated on the third or fourth day after operation. We observed an inward movement of the catheter in 56% of the patients instead of the expected outward movement. This inward movement was accompanied by a higher level of sensory blockade. No relationship with radiological visualisation was found.*

## Key words

*Anaesthetic techniques, regional*; epidural.
*Equipment*; catheters, epidural.

Care must be taken when long-term epidural catheters are used in case they change their position in the epidural space. Inadequate analgesia or complete failure is commonly seen when catheters have moved outwards. More frightening is a migration inwards into the subdural space that results in a total spinal.[1–4] It was found, in a study on epidural catheter migration during labour, that twice as many catheters moved inwards as out.[5] Migration through an intervertebral foramen may result in a patchy block or inadequate analgesia.[6]

The purpose of this study was to determine the incidence, magnitude and direction of catheter migration when sited at a high thoracic level and its clinical relevance.

### Methods

The study was approved by the hospital ethics committee and informed consent was obtained from each patient. Patients with a history of allergy to local anaesthetics or radiopaque dye were only partially studied. All patients were scheduled for thoracic surgery and pleural drainage with 3.0 kPa suction when necessary postoperatively.

Epidural catheters were introduced prior to surgery with the patient in the sitting position. A 16-gauge Touhy needle was inserted via a paramedian approach at the $T_{3-4}$ or $T_{4-5}$ level and the space located using the hanging drop technique. The needle orifice was directed cephalad and a catheter inserted 4 cm. The catheter had three side holes at 0.5, 1.0 and 1.5 cm from the distal end and was marked with lines and blocks for the determination of its depth. A record was made of the depth of the catheter at the skin level. All catheters were fixed in place in the same way: looped on the patient's back and fixed with consecutive layers of Duoderm, Mefix and Tegaderm. Duoderm is a hydro-active wound dressing with adhesive properties; Mefix is an adhesive plaster; Tegaderm is an impermeable adhesive plastic which prevents soiling with blood from the surgical field.

A test dose of 2% plain lignocaine 3 ml or 0.375% plain bupivacaine 3 ml was given. The patient was then turned into the supine position and the sensory blockade assessed by response to pinprick 10 minutes after lignocaine and 15 minutes after bupivacaine. Epidural analgesia with 6 to 8 ml bupivacaine 0.5% together with adrenaline 5 μg/ml was used to supplement general anaesthesia.

Twenty-four patients received 300 mg/ml iohexol 1 ml (Omnipaque 300) via the epidural catheter after the operation, and a chest X ray.

Postoperative pain relief was obtained with continuous epidural infusion of either nicomorphine (niconylmorphine, a narcotic analgesic) or sufentanil. Bupivacaine 0.125% was added if pain relief was insufficient. The epidural infusion was stopped 8 hours before the second test dose of the local anaesthetic. No intravenous opioids were administered.

---

J. Mourisse, MD, M.J.M. Gielen, MD, PhD, M.A.W.M. Hasenbos, MD, PhD, Department of Anaesthesia, F.M.J. Heystraten, MD, PhD, Department of Radiology, St Radboudhospital, Postbox 9101, 6500 HB Nijmegen, The Netherlands.
Correspondence should be addressed to Dr J. Mourisse please.

Accepted 11 January 1988.

0003–2409/89/070574+04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

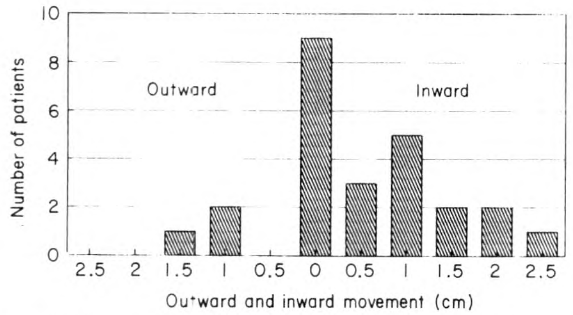


**Fig. 1.** Catheter migration; distribution of skin level differences. Total number of patients: 25.

Three or four days after the insertion of the epidural catheter a test dose of local anaesthetic, similar to that delivered on the first day, was given at the same injection speed and assessed in the same way. Radiopaque dye was also injected and a chest X ray taken. Afterwards the adhesive dressing was carefully removed and the depth of the catheter at skin level assessed. Catheter migration was defined as the difference in skin levels between the moment of catheter insertion and its removal.

For statistical analysis the Pearson correlation and the Chi-squared test were used. Values of $p < 0.05$ were considered as significant.

## Results

Twenty-five epidural catheters were evaluated. Nineteen were inserted at the $T_{3-4}$, five at the $T_{4-5}$ and one at the $T_{2-3}$ interspace. The depth from skin to the epidural space ranged from 5.7 to 8.5 cm. Nine patients received lignocaine for the test dose. Twenty-three of the 25 patients underwent lateral thoracotomy, two had a thoracic cage repair and another also had a median sternotomy. Four patients had their epidural catheter in place for 3 days and 21 patients for 4 days. All patients had good peroperative and postoperative pain relief except one who needed the addition of a local anaesthetic agent.

Patient data are shown in Table 1. Patient number 13 had her epidural catheter removed before final testing could be done; patient 14 had an obstructed epidural catheter and patient 15 had a history of an allergic reaction to radiopaque dye.

The range of catheter migration is shown in Figure 1. The catheter had not moved from its original position in nine patients; in three it had moved outwards and in 13 patients inwards. There was an inward movement in 56% of the patients.

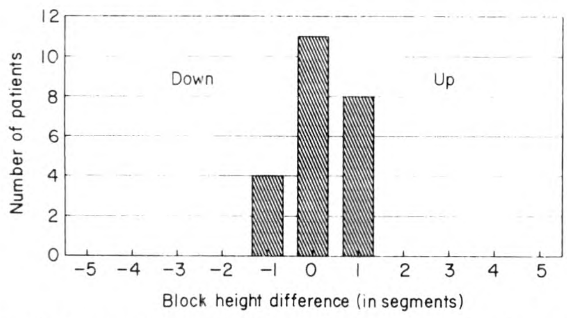


**Fig. 2.** Sensory blockade; distribution of upper block height differences. Total number of patients: 23.

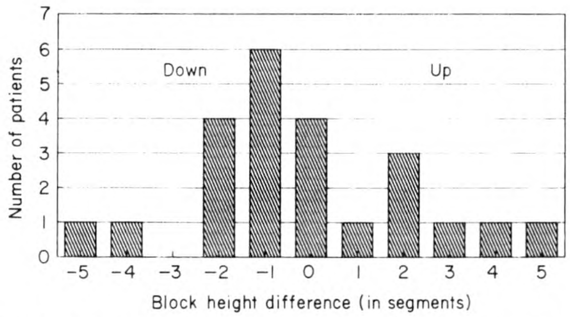


**Fig. 3.** Sensory blockade; distribution of lower block level differences. Total number of patients: 23.

Figures 2 and 3 show the distribution of the block height differences for the upper and lower borders of the sensory blockade between first and second test. To simplify the findings the mean block height between left and right was used. There was an elevation of the upper border of the sensory blockade in eight patients; in 11 there was no difference and in four it was lower. The range of upper block differences was much narrower than the lower.

Figure 4 shows the distribution of the difference in catheter tip position, visualised by the radiopaque dye. There was a cephalad movement of the catheter tip in only two patients (numbers 19 and 20, Table 1) and a caudad migration in three (9, 11 and 16).

The correlation between catheter migration and upper block height difference was significant, whereas the correlation between catheter migration and lower block height difference was not significant. There was no correlation with catheter migration with either upper or lower block height difference, when the radiological visualisation of the catheter tip was examined.

There was no significant difference in the number of catheters that migrated in or out when sited at $T_{3-4}$ or $T_{4-5}$, nor could any relation be found between catheter migration and depth of the epidural space, nor with the Broca-index (length in metres, weight in kg,). There was no relation either between catheter migration and use of 3.0 kPa suction pressure to the pleural suction drains, between catheter migration and choice of local anaesthetic, or between choice of local anaesthetic and height of the block.

## Discussion

For many years anaesthetists have looked for the best way to fix an epidural catheter to the patient's back. The problems with most types of adhesive plasters were premature loosening and kinking of the catheter. Duoderm in

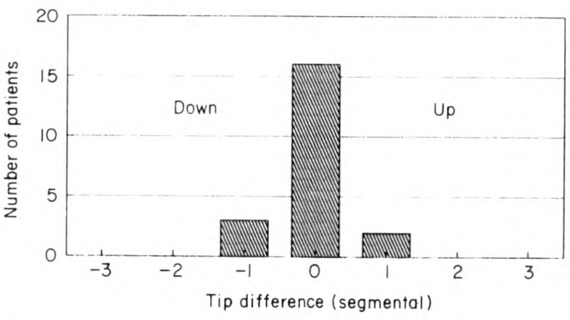


**Fig. 4.** Radiological visualisation; distribution of tip position differences. Total number of patients: 21.

Table 1. Patient data.

| Number | Sex | Age (years) | Weight (kg) | Height (cm) | Suction (Y/N) | Level of insertion (T) | First skin level (cm) | Second skin level (cm) | First block right (T) | First block left (T) | Second block right (T) | Second block left (T) | First tip (T) | Second tip (T) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 72 | 69 | 172 | Y | 3–4 | 9.00 | 9.60 | 3– 5 | 2– 6 | 2– 6 | 2– 6 | 3 | Not visible |
| 2 | M | 66 | 75 | 179 | N | 3–4 | 8.50 | 7.50 | 1– 6 | 1– 6 | 2– 5 | 2– 5 | 4 | 4 |
| 3 | M | 56 | 90 | 177 | Y | 3–4 | 11.00 | 11.00 | 3– 8 | 2– 9 | 3– 6 | 3– 6 | 3 | 3 |
| 4 | M | 65 | 70 | 170 | Y | 3–4 | 10.50 | 10.70 | 2– 6 | 2– 6 | 2– 7 | 2– 7 | 3 | 3 |
| 5 | F | 55 | 62 | 162 | Y | 3–4 | 10.70 | 10.70 | 2–10 | 2–10 | 2–10 | 2–10 | 2 | 2 |
| 6 | M | 73 | 90 | 175 | Y | 4–5 | 7.70 | 8.60 | 2– 6 | 3– 7 | 2–10 | 2–10 | 4 | 4 |
| 7 | M | 79 | 68 | 169 | Y | 3–4 | 10.00 | 11.30 | 2–10 | 2–10 | 2– 6 | 2– 6 | 3 | 3 |
| 8 | M | 58 | 75 | 165 | Y | 2–3 | 10.70 | 10.70 | 2–10 | 2–10 | 2– 5 | 2– 6 | 2 | 2 |
| 9 | F | 56 | 73 | 173 | Y | 4–5 | 10.70 | 11.70 | 2– 6 | 2– 6 | 2– 6 | 2– 6 | 2–3 | 3 |
| 10 | F | 69 | 45 | 160 | N | 3–4 | 8.50 | 8.50 | 2– 6 | 2– 9 | 3– 6 | 2– 6 | 3 | 3 |
| 11 | M | 27 | 65 | 178 | Y | 3–4 | 9.50 | 11.70 | 2– 6 | 2– 7 | 1– 6 | 2–11 | 5 | 5–6 |
| 12 | F | 76 | 71 | 161 | Y | 3–4 | 8.50 | 9.00 | 3– 5 | 3– 5 | 2– 6 | 2– 7 | 3 | 3 |
| 13 | F | 44 | 62 | 154 | Y | 4–5 | 9.50 | 10.50 | 2– 6 | 2– 6 | — | — | 4 | — |
| 14 | M | 79 | 60 | 161 | Y | 3–4 | 12.00 | 12.50 | 2– 6 | 3– 5 | — | — | 2 | — |
| 15 | M | 74 | 95 | 173 | Y | 3–4 | 10.70 | 13.00 | 2– 6 | 2– 6 | 2– 6 | 2– 6 | — | — |
| 16 | M | 48 | 82 | 180 | Y | 3–4 | 12.00 | 13.30 | 2– 5 | 2– 5 | 2– 6 | 2– 6 | 2–3 | 3 |
| 17 | M | 63 | 87 | 175 | Y | 3–4 | 11.30 | 10.50 | 2– 5 | 2– 5 | 2– 9 | 2–10 | 4 | 4 |
| 18 | F | 48 | 77 | 165 | Y | 4–5 | 12.50 | 13.50 | 2– 6 | 2– 6 | 1– 8 | 3– 7 | 4 | 4 |
| 19 | M | 57 | 76 | 182 | Y | 3–4 | 10.70 | 10.70 | 3– 5 | 3– 5 | 3– 5 | 3– 5 | 3 | 2 |
| 20 | M | 71 | 86 | 190 | Y | 4–5 | 9.50 | 9.50 | 3– 6 | 3– 6 | 3– 7 | 3– 7 | 5 | 4–5 |
| 21 | F | 70 | 63 | 160 | Y | 3–4 | 12.40 | 10.70 | 1–10 | 1–10 | 2– 7 | 2– 9 | 3 | 3 |
| 22 | M | 57 | 59 | 177 | N | 3–4 | 11.50 | 12.50 | 2– 5 | 2– 5 | 1– 6 | 1– 6 | 1 | 1 |
| 23 | M | 56 | 75 | 170 | Y | 3–4 | 12.50 | 14.30 | 3– 5 | 3– 5 | 2– 7 | 2– 7 | 3 | 3 |
| 24 | M | 14 | 58 | 178 | N | 3–4 | 9.50 | 9.50 | 1– 5 | 2– 6 | 1– 6 | 1– 6 | 4 | 4 |
| 25 | F | 17 | 66 | 169 | Y | 3–4 | 9.50 | 9.50 | 2– 6 | 2– 7 | 1– 5 | 1– 5 | 3 | 3 |

combination with Mefix decreased the number in whom the catheters came out altogether. Only a few migrated outwards and surprisingly we found that most of them migrated inwards (56%). This inward movement is possible because the Duoderm becomes softer at skin temperature. Phillips *et al.*[5] found that 36% catheters at the lumbar level moved inwards, but in their study, fixing the catheter was not standardised and they used several kinds of adhesive plaster.

The causes of the inward movement of an epidural catheter are still hypothetical. It is thought it results from subatmospheric epidural pressure. Usubiaga *et al.*[7] showed that this pressure consisted of two components, namely a subatmospheric pressure exaggerated by flexion of the spine, and superimposed on this basal value, oscillations synchronous with respiration at the thoracic level; the pressure becomes more subatmospheric during inspiration. Suction to the pleural space in most of our patients was used, but there was no relationship between this and catheter migration.

Another possibility was proposed by Phillips *et al.*[5] They suggested that catheter migration was due to the gripping action of the ligamentum flavum which propels the catheter inwards as the patients straighten their backs from the flexed position adopted for its insertion. Yet another possibility is that a catheter only seems to go inwards because of the swelling of the subcutaneous tissues by oedema, local infiltrates or subcutaneous emphysema. There were no such changes in our study at the puncture sites. It was also found that if the catheter moved inwards, there was a significant increase in the upper block height. This indicates the migration took place into the epidural space.

How can one diagnose a catheter migration? It is clear it can be seen when the length of the catheter inside the patient is monitored, but with the fixing method this is only possible when the adhesive plaster is removed.

A relation between catheter migration and upper block height difference was found in our study. Thus an increase in upper block height could be due to inward catheter migration. But why only the upper block height and not the lower block level? This is probably because of the shape of the epidural space in the thoracic region; it is triangular with the apex directed cephalad and the base caudad.[8] A bolus of fluid will tend to flow towards the base of the triangle. This may be seen in Figures 2 and 3; the upper block height difference had a much narrower range than the lower level. The only way to obtain a higher block with the same amount of fluid is to move the catheter tip higher.

Radiological visualisation seems to have little value for the estimation of catheter migration. This was partly the result of the poor ability of the bedside X ray to visualise the tip of the catheter and to the differences in projection between the first and last days. On the first day the patients lay flat on the bed while on the last day they were sitting. Another problem was the inability to control at which orifice of the catheter the contrast dye would flow out.[9,10] This can also be important in the evaluation of the test dose. The speed of injection has to be standardised.[9] These problems make it difficult to tell whether a catheter tip has moved upwards or downwards. In a study by Slappendel *et al.*[11] there was no relationship between block height and radiological evaluation, which was confirmed by our findings. We encountered no problems with migration of catheters into the subdural space, into an epidural vessel or through an intervertebral foramen.

In conclusion, one should monitor the depth of catheter beneath the skin, which could be facilitated by the use of transparent adhesive dressing. This can be supplemented by occasionally checking the height of the block in response to a standard test dose of local anaesthetic. There is no advantage in using radiological confirmation of catheter tip position to evaluate possible catheter migration.

## Acknowledgments

We thank Dr P. Allen for manuscript correction and Dr J. Van Egmond for his help with the statistical analysis.

## References

1. Boys JE, Norman PF. Accidental subdural analgesia: a case report, possible clinical implications and relevance to 'massive extradurals'. *British Journal of Anaesthesia* 1975; **47:** 1111–3.
2. Philip JH, Brown WU. Total spinal anesthesia late in the course of obstetric bupivacaine epidural block. *Anesthesiology* 1976; **44:** 340–1.
3. Park R. A migrating epidural cannula. *Anaesthesia* 1984; **39:** 289.
4. Phillips DC, MacDonald R, Lyons G. Possible subarachnoid migration of an epidural catheter. *Anaesthesia* 1986; **41:** 653–4.
5. Phillips DC, MacDonald R. Epidural catheter migration during labour. *Anaesthesia* 1987; **42:** 661–3.
6. Sanchez R, Acuna J, Rocha F. An analysis of the radiological visualization of the catheters placed in the epidural space. *British Journal of Anaesthesia* 1967; **39:** 485–9.
7. Usubiaga JE, Moya F, Usubiaga LE. A note on the recording of epidural negative pressure. *Canadian Anaesthetists' Society Journal* 1967; **14:** 119–22.
8. Park WY. Factors influencing distribution of local anesthetics in the epidural space. *Regional Anesthesia* 1988; **13:** 49–57.
9. Power I, Thorburn J. Differential flow from multihole epidural catheters. *Anaesthesia* 1988; **43:** 876–8.
10. Kumar CM, Dennison B, Lawler PGP. Excessive dose requirements of local anaesthetic for epidural analgesia. How far should an epidural catheter be inserted? *Anaesthesia* 1985; **40:** 1100–2.
11. Slappendel R, Gielen MJM, Hasenbos MAWM, Heystraten FMJ. Spread of radiopaque dye in the thoracic epidural space. *Anaesthesia* 1988; **43:** 939–42.

*Anaesthesia*, 1989, Volume 44, pages 578–580

# A comparison between open-end (single hole) and closed-end (three lateral holes) epidural catheters

## Complications and quality of sensory blockade

S. MICHAEL, M. N. RICHMOND AND R. J. S. BIRKS

**Summary**

*A randomised, single-blind study was conducted on 802 parturient women who required epidural analgesia, to compare open-end (single hole) with closed-end (three lateral holes) epidural catheters. The complication rate after catheter insertion was not statistically different between the two groups, but the number of unsatisfactory blocks was significantly higher in the open-end group ($p < 0.001$). The closed-end catheters were easier and less painful to place, but gave a higher incidence of bloody taps. The open-end catheters caused sensory blockade to be more frequently unilateral and more frequently missed sensory segments. This resulted in a significantly higher number of open-end catheters that required replacement ($p < 0.001$). Open-end catheters despite their theoretical advantages in the detection of intravenous and subarachnoid placement caused an unacceptably high incidence of unsatisfactory sensory blockade.*

**Key words**

*Equipment*; catheters, epidural.
*Anaesthetic techniques, regional*; epidural.

Epidural analgesia is the most successful method of pain relief in labour but can, at times, be difficult to achieve. The failure rate, even in skilled hands, may be as high as 8%.[1] This may be attributed to poor technique, but may also be due to the abnormal placement of the epidural catheter passed through a successfully placed epidural needle.[2] Such abnormal placement includes blocked,[3] kinked[4] or bent catheters, deviation through an intervertebral foramen, passage into an epidural vein, the subdural or the subarachnoid space.[5]

Epidural catheter design may influence the successful outcome of epidural analgesia. The commonly used closed-end (three lateral holes) catheters are recognised to present potential problems with multicompartmental placement, i.e. different holes lying within different anatomical spaces.[5] Open-end single-hole catheters do not present this complication, but are, however, more likely to become blocked especially by blood clot.[3]

This present study compared two different catheter designs and aimed to identify any difference in the incidence of complications of catheter insertion and any difference in the quality of sensory blockade.

## Methods

Eight hundred and two parturient women who required epidural analgesia were studied, after Ethics Committee approval and written, informed consent. The mothers were aged between 16 and 40 years, ASA grade 1 or 2 and were not taking any concurrent medication. A closed method was used to allocate the patients randomly into two groups, one to receive open-end and the other closed-end catheters. The study was not double-blind. The anaesthetist was aware which catheter type was inserted, but the mother and accompanying midwife were not. Both catheter types used were made by Portex Ltd.

An intravenous infusion of 500 ml normal saline was given to all mothers prior to performance of the epidural block, which was sited with the mother lying in the left lateral position using a midline approach and a loss of resistance to saline technique. The open-end catheters were inserted 1.5 cm and the closed-end catheters 2.5 cm beyond the tip of the Tuohy needle after identification of the epidural space. Any complications of catheter insertion were noted at this stage, namely difficulty in passing the catheter (difficult), nerve root pain or paraesthesiae experienced by the patient (painful), epidural vein puncture (bloody tap) and dural puncture (dural tap).

The position of the catheter was checked and fixed to the skin. The midwife was then asked to monitor the mother's radial pulse and a test dose of 0.5% bupivacaine 2 ml with 1:200 000 adrenaline was injected into the epidural space. The general condition and pulse were monitored for 2 minutes to detect signs of intravenous injection. This was

S. Michael, MB, ChB, FFARCSI, Lecturer in Anaesthesia, University Department of Anaesthesia, Medical School, Beech Hill Road, Sheffield, S10 2RX, M.N. Richmond, MB, ChB, FFARCS, R.J.S. Birks, MB, ChB, FFARCS, Consultants, Jessop Hospital for Women, Leavygreave Road, Sheffield, S3 7RE.

Accepted 24 January 1988.

0003–2409/89/070578+03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

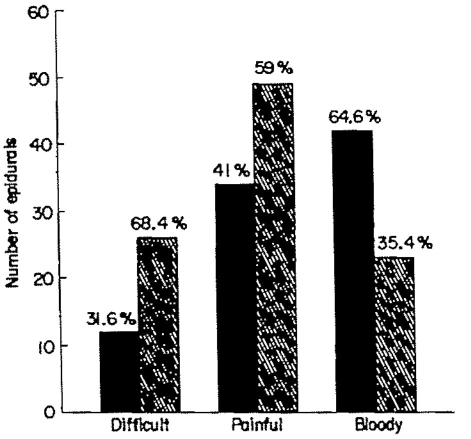


**Fig. 1.** Complications according to type of catheter. ■, closed end; ▨, open end.

followed at 5 minutes by an assessment to exclude subarachnoid injection. A slow injection of 0.25% bupivacaine 8 ml was then given over 2 minutes. The mother was rolled from the left to the right lateral position after a further 5 minutes. The maternal heart rate, arterial blood pressure and fetal heart rate were recorded at 5-minute intervals for 20 minutes.

The mother and midwife were asked to comment on the quality of pain relief 30 minutes after the injection of the main dose of bupivacaine. Sensation was then tested by the anaesthetist, using ethyl chloride spray. Confirmed unsatisfactory sensory blockade was classified as unilateral blockade with an unsatisfactory effect on the contralateral side (unilateral), missed sensory dermatomes (missed segments) and inadequate caudal or cephalad spread of the blockade (incomplete). Mothers who continued to complain at 40 minutes were managed initially by an additional dose of 0.125% bupivacaine 16 ml and subsequently, if this was unsuccessful, by resiting the epidural catheter.

Statistical analysis used a Chi-squared test to compare the two groups for complications of catheter insertion, quality of sensory blockade and the numbers of epidural catheters resited.

## Results

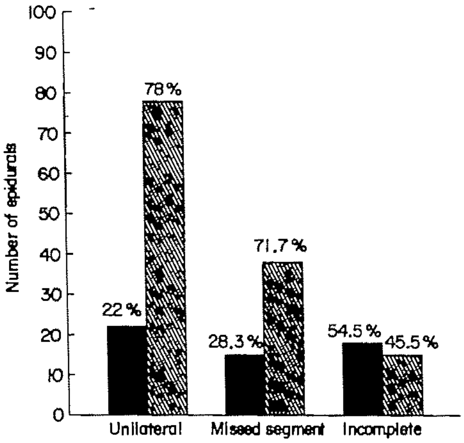


**Fig. 2.** Unsatisfactory blocks according to type of catheter. ■, closed end; ▨, open end.

The results are shown in Table 1 and Figures 1 and 2. Inadvertent dural taps occurred in two mothers during Tuohy needle insertion, but no dural puncture occurred during catheter insertion. There were no instances of intravenous or subarachnoid injection of bupivacaine. Twenty-seven epidurals were resited after the criteria for unsuccessful analgesia described above were met. Twenty-three of these were in the open-end and four in the closed-end group ($p < 0.001$).

**Table 1.** Number of complicated and unsatisfactory blocks, type of complication and quality of blockade related to catheter type.

| | Closed-end | Open-end |
|---|---|---|
| Number | 401 | 401 |
| Complicated | 88 | 98 |
| Complications | | |
| Difficult | 12 | 26 |
| Painful | 34 | 49 |
| Bloody tap | 42 | 23 |
| Dural tap | 0 | 0 |
| Unsatisfactory | 55 | 131 |
| Quality of blockade | | |
| Unilateral | 22 | 78 |
| Missed | 15 | 38 |
| Incomplete | 18 | 15 |

### *Complications*

There was no statistically significant difference between the two groups in the number of epidurals with complications. Eighty-eight out of 401 had complications in the closed-end group compared to 98 out of 401 in the open-end group. Figure 1 shows the type of complications. Difficult and painful placement was more common with open-end catheters and bloody taps more common with closed-end catheters. Twenty-six out of 38 (68.4%) catheters difficult-to-place and 49 out of 83 (59%) painful-to-place were of the open type. Forty-two out of 65 (64.6%) bloody taps occurred with closed-end catheters.

### *Quality of sensory blockade*

There was a highly significant difference between the two groups regarding quality of sensory blockade. Thus 55 out of 401 in the closed-end group and 131 out of 401 in the open-end group were unsatisfactory ($p < 0.001$). The types of unsatisfactory block are shown in Table 1 and Figure 2. Unilateral blocks and missed segments were more frequently associated with open-end catheters and incomplete blocks with closed-end catheters. Seventy-eight out of 100 (78%) unilateral blocks and 38 out of 53 (72%) missed segments occurred with open-end catheters. Eighteen out of 33 (54.5%) incomplete blocks occurred with closed-end catheters.

## Discussion

Safety is of paramount consideration in the delivery of an epidural service. Intravenous or subarachnoid injection of a large volume of a local anaesthetic drug can be fatal. Open-end catheters should, in theory, make incorrect placement easier to detect since their hole can only lie in one anatomical space.[5,6] Closed-end catheters can present diagnostic difficulties in incorrect placement and potentially lead to accidental intravenous or subarachnoid injection.[7] Multicompartmental placement has been shown to occur at alarming levels and some authors have condemned the use of closed-end, multihole, catheters.[5]

There were no cases of inadvertent intravenous or subarachnoid injection in our study, which was not unexpected since the incidence of these complications is very low.[8] Two dural taps were accidentally performed with the Tuohy needle, a frequency which is in agreement with other reports,[9] but no catheters were placed in the subarachnoid space.

Closed-end catheters were more frequently placed intravenously but were all recognised immediately and corrected by appropriate adjustment. A possible explanation of this is that despite the fact that both catheter types puncture vessels with equal frequency, the probability that one of the three holes of a closed-end catheter might lie in a vessel is higher than the single hole of an open-end catheter. Open-end catheters gave rise to difficult and painful placement more frequently than closed-end ones. This may be due to catheter tip design, since open-end catheters do not have a smooth tip and thus may traumatise other structures during placement. The sharper tip could also make open-end catheters more likely to penetrate the dura or blood vessels.

Quality of sensory blockade and satisfactory analgesia are also important considerations of an epidural service. Consistent success rates have earned epidurals a high reputation in the United Kingdom. The significantly higher number of unsatisfactory blocks recorded in our study in the open-end group is difficult to accept, especially since a significant number of these epidurals had to be resited.

Most of the unsatisfactory blocks were unilateral, and open-end catheters accounted for 78% of these. This is in agreement with previous observations, but as a proportion of the overall number our figure of 19.5% is much higher than the previously quoted 12%.[9] Unilateral blocks are presumably caused by the catheter tip and hole lying on one side of the midline making spread of the solution to the other side difficult.

Missed segments were also more frequently associated with open-end catheters and were probably due to malposition of the catheter tip within the epidural space; this prevents adequate spread of the local analgesic. Incomplete blocks were approximately equally distributed between the two groups.

In conclusion, we note that open-end catheters still have a theoretical advantage over the closed-end in the prevention of serious complications of epidural analgesia. This however was not demonstrated by our study. Meticulous technique should eliminate potential problems so that closed-end catheters (with three lateral holes) can continue to be used and give better pain relief.

## Acknowledgments

We thank our anaesthetic colleagues and the midwifery staff on Labour Ward at the Jessop Hospital for Women, for their assistance during this study.

## References

1. DUCROW M. The occurrence of unblocked segments during continuous lumbar epidural analgesia for pain relief in labour. *British Journal of Anaesthesia* 1971; **43:** 1172–4.
2. CRAWFORD JS. *Principles and practice of obstetric anaesthesia,* 4th edn. Oxford: Blackwell Scientific 1978.
3. SCOTT DB, WILSON J. Insertion of epidural catheters. *Anaesthesia* 1983; **38:** 1108–9.
4. KUMAR CM, DENNISON B, LAWLER PGP. Excessive dose requirements of local anaesthetic for epidural analgesia. How far should an epidural catheter be inserted? *Anaesthesia* 1985; **40:** 1100–2.
5. BECK H, BRASSOW F, DOEHN M, BAUSE H, DZIAZKA A, SCHULTE AM, ESCH J. Epidural catheters of the multi-orifice type: dangers and complications. *Acta Anaesthesiologica Scandinavica* 1986; **30:** 549–55.
6. PHILLIPS DC, MACDONALD R. Epidural catheter migration during labour. *Anaesthesia* 1987; **42:** 661–3.
7. HARTLEY M. The strange case of the inadvertent spinal. *British Journal of Anaesthesia* 1975; **47:** 420.
8. MOIR DD, THORBURN J. *Obstetric Anaesthesia and analgesia,* 3rd edn. London: Balliere Tindall, 1986.
9. JUSTINS DM. The relief of pain in labour. In: CHURCHILL-DAVIDSON HC, ed. *A practice of anaesthesia,* 5th edn. London: Lloyd-Luke, 1984.

*Anaesthesia*, 1989, Volume 44, pages 581–584

# The requirement for intensive care support for the pregnant population

S. G. GRAHAM AND M. C. LUXTON

## Summary

*Pregnancy-associated admissions to the Intensive Care Unit during the first 5 years of a newly established teaching hospital obstetric unit are reviewed. There were 23 such admissions; in the same period, 21 983 deliveries occurred. The most frequent cause for Intensive Care admission was hypertensive disease of pregnancy. Most patients required admission for less than 48 hours. Two patients died during the period of study.*

**Key words**

*Intensive care*; obstetric.
*Blood pressure*; hypertension.

Obstetric services were established in the Queen's Medical Centre (QMC), the new teaching hospital in Nottingham, on 1 January 1982, as part of a phased programme of development. The unit was derived from the transfer of the obstetric units from the Hospital for Women in Nottingham, and the University Department of Obstetrics and Gynaecology from the City Hospital, Nottingham.

Obstetric units have a recognised requirement for anaesthetic input into patient management, the general pattern of which has been described elsewhere.[1] Severe illness may occur coincidentally with, or as a consequence of, pregnancy. Many of these patients are managed satisfactorily on labour suites or on appropriate wards, but the more critically ill may require admission to an Intensive Care Unit (ICU).

This review seeks to examine the demand that this pregnant population has made on the Intensive Care facilities at Queen's Medical Centre.

## Methods

The study population was defined as those patients who required admission to the ICU between 1 January 1982 and 31 December 1986, with an established pregnancy of gestational age greater than 20 weeks, or whose admission was the direct result of pregnancy and in the same hospital admission as the delivery. The medical records of all patients who fulfilled these criteria were obtained and analysed. Admission data for this period were obtained from the labour suite records.

The data derive mainly from the period of admission to ICU. Discharge status, for example, refers to status at the time of discharge from the ICU unless stated otherwise. Progress after discharge was examined and is presented where relevant.

## Results

A total of 21 983 obstetric deliveries took place during the study period in the labour suite and associated areas of the QMC. There were 23 pregnancy-associated admissions to the ICU over this same period, each in separate pregnancies. One patient was admitted twice to the ICU in successive pregnancies; the causes for these admissions were probably unrelated. Table 1 shows admission data on an annual basis.

The reasons for admission to ICU are listed in Table 2. One patient with severe pre-eclampsia suffered a placental abruption, which gave rise to the need for her admission, and consequently she appears twice in the totals. No pregnancy-associated deaths occurred during the study period outside the ICU but within the QMC.

### *Anaesthetic causes for ICU admission*

One patient presented as a difficult intubation, and required mechanical ventilation postoperatively for 12 hours for respiratory failure. Initially, her trachea was extubated satisfactorily, but she failed to progress and required reintubation and a further period of mechanical ventilation. An initial chest X ray on the ICU suggested the possibility of bilateral basal collapse, but after overnight

S.G. Graham, MB, ChB, Registrar, M.C. Luxton, BM, BCh, FFARCS, Consultant, Department of Anaesthetics, Queen's Medical Centre, Clifton Boulevard, Nottingham, Notts NG7 2UH.

Accepted 1 February 1989.

0003–2409/89/070581+04 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Comparison of labour suite and pregnancy-associated ICU admissions. Figures in parentheses are percentages of the 5-year totals.

| Year | Obstetric deliveries | Pregnancy-associated ICU admissions |
|---|---|---|
| 1982 | 3875 (17.6) | 4 (17.4) |
| 1983 | 4330 (19.3) | 5 (21.7) |
| 1984 | 4466 (20.3) | 1 (4.3) |
| 1985 | 4667 (21.2) | 6 (26.1) |
| 1986 | 4645 (21.1) | 7 (30.4) |

ventilation with positive end-expiratory pressure (PEEP) and physiotherapy her trachea was extubated uneventfully and she returned to the ward.

One patient had a stormy anaesthetic course, with a labile blood pressure intra-operatively, and respiratory insufficiency afterwards. No cause could be attributed to this at the time. She was diagnosed as suffering from dystrophia myotonica 18 months later. The third patient had an anaphylactoid reaction to one of the agents used for induction of anaesthesia during an emergency Caesarean section for fetal distress.

### *'Other' causes for ICU admission*

One patient in whom the fetus died *in utero* developed severe disseminated intravascular coagulopathy (DIC), and was admitted for monitoring and treatment.

One patient developed DIC after a Caesarean section for fetal distress. She was admitted again during a subsequent pregnancy. She developed spinal cord compression caused by a haemangioma, and underwent Caesarean section and thoracic laminectomy at 34 weeks' gestation and was admitted for postoperative observation.

Another patient developed laryngeal carcinoma during her pregnancy. She developed severe respiratory insufficiency during diagnostic laryngoscopy, and an emergency tracheostomy was performed. She was admitted to ICU for postoperative observation, and subsequently underwent Caesarean section and laryngectomy.

### *Duration of support*

Thirteen of the 23 patients (56%) remained on the ICU for less than 48 hours. The mean duration of stay was 4.1 days (Fig. 1).

Fourteen patients (60.9%) required ventilatory support, and PEEP was used in seven of these. The mean duration of mechanical ventilation was 2.7 days (Fig. 2).

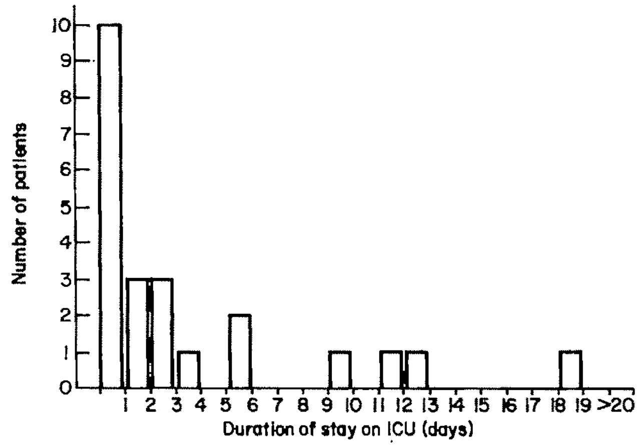


**Fig. 1.** Duration of intensive care for severe pregnancy-associated illness.

### *Cardiovascular monitoring*

All the patients admitted to ICU in this study had an indwelling intra-arterial cannula inserted for direct arterial pressure monitoring and arterial blood gas sampling. A central venous cannula was inserted in 14 patients (60.9%). A flow directed pulmonary artery catheter was inserted in four of these patients (28.6% of the subgroup). The indication for central venous pressure monitoring was circulatory instability; this was associated in most cases with hypertensive diseases of pregnancy, but other causes were massive haemorrhage and DIC. Central venous lines were inserted either intra-operatively to provide adequate monitoring, or postoperatively to indicate the adequacy of fluid resuscitation in a hypotensive oliguric patient who failed to respond to a simple fluid challenge. Pulmonary artery catheters were sited in order to distinguish between raised pulmonary vascular resistance or primary left heart failure in hypotensive patients with an 'adequate' central venous pressure. Three of the patients who required pulmonary artery catheterisation had eclampsia or pre-eclampsia, and the other had bled profusely and suffered a cardiac arrest during the operative procedure.

Inotropic support was given to five patients, using dopamine in doses between 5 and 15 $\mu$g/kg/minute, as a response to the information obtained from invasive monitoring.

### *Coagulation*

A coagulopathy is a well recognised, potentially life-threatening complication of hypertensive diseases of pregnancy,

**Table 2.** Reasons for pregnancy-associated ICU admission, and deaths associated with these admissions. Percentages of total maternal mortality in each subgroup between 1970 and 1981[2] are shown for comparison.

| Cause of ICU admission | Admissions (% of total) | Deaths (% of admissions) | 1970–1981 maternal mortality (% of total) |
|---|---|---|---|
| Hypertensive diseases of pregnancy | 13 (56.5) | 2 (8.6) | 13.3–20.4 |
| Anaesthesia | 3 (13.0) | 0 | 10.9–13.2 |
| Placental abruption | 3 (13.0) | 0 | 2.1–3.7 |
| Haemorrhage | 1 (4.3) | 0 | 7.9–11.0 |
| Other causes | 4 (17.4) | 0 | N/A |

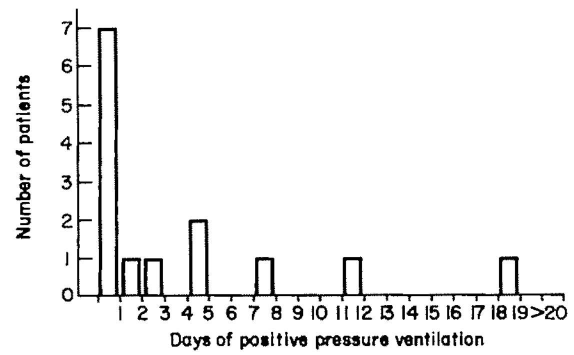


**Fig. 2.** The requirement for mechanical ventilation in pregnancy-associated ICU admissions.

placental abruption, severe haemorrhage, and intra-uterine fetal death. Any coagulopathy was grouped into one of four categories, depending on the need for therapeutic intervention. These data are presented in Table 3. Most patients did not display a coagulopathy, or did not require correction of the minor abnormalities demonstrated, but five patients (21.7%) required correction of a severe coagulopathy.

### *Hypertensive diseases of pregnancy*

There were no specific criteria for admission of the hypertensive patients to ICU. The decision was taken by the obstetric anaesthetist. Many factors contributed to the decision to admit these patients; these included severe intra-operative cardiovascular instability, significant blood loss, a decision by the duty anaesthetist to institute elective postoperative ventilation, and potential difficulty with provision of appropriate monitoring facilities (including inadequate staffing levels) in a busy delivery suite.

A central venous catheter was inserted in 12 of these patients and a pulmonary artery catheter was inserted in three. Four patients required inotropic support.

Mechanical ventilation was deemed appropriate for 10 of these patients for periods ranging from 12 hours to 19 days. Of the total of five patients who required ventilation for 5 days or more, four had pregnancy-induced hypertension (three with ARDS, one with laryngeal oedema).

Five patients in this group developed a coagulopathy which required treatment with blood products; this treatment was guided by the Department of Haematology. Most of these patients followed the expected pattern for this condition, stabilised rapidly after delivery, and were discharged to the ward within 48 hours.

### *Adult respiratory distress syndrome (ARDS)*

The overall incidence of ARDS is difficult to ascertain with certainty. Only three patients were given the diagnostic label of ARDS, and the requirement for ventilatory support in the other patients can be explained on other grounds. It is our belief therefore that the overall incidence of ARDS was not greatly in excess of 3/23 admissions (13%). All three suffered from pregnancy-induced hypertension, and two also developed DIC; it was assumed that this formed the origin of the ARDS.

**Table 3.** Requirement for correction of coagulopathy in pregnancy-associated ICU admissions.

| Blood product requirement | No. of patients | % of total |
|---|---|---|
| Normal coagulation tests | 14 | 60.9 |
| Some coagulopathy, no correction required | 0 | 0 |
| < 4 units required | 4 | 17.4 |
| > 4 units required | 5 | 21.7 |

**Table 4.** Outcome of pregnancy-associated ICU admissions.

| Discharge status | No. of patients | % of total |
|---|---|---|
| Normal/near normal | 15 | 65.3 |
| Slight disability | 2 | 8.7 |
| Moderate disability | 4 | 17.4 |
| Died | 2 | 8.7 |

### *Outcome*

Fifteen of the patients who required ICU admission achieved near full recovery at the time of discharge (Table 4). Two patients had a slight residual disability. One patient with eclampsia had a resolving hemiparesis and a slight visual field defect at the time of discharge; her neurological deficit preceded her admission to the ICU. The other patient had no obvious problems at the time of her discharge, but is included here because of the possibility that her subsequently diagnosed dystrophia myotonica may have contributed to her admission.

Four patients were classified as having a moderately severe disability. One patient who had spinal cord compression caused by a haemangioma was discharged with a resolving paraplegia. One patient with placenta praevia and severe intra-operative bleeding suffered a cardiac arrest, required an emergency hysterectomy and had a stormy postoperative course. She required repeated surgical re-exploration and developed a vesicovaginal fistula which has since been repaired. In addition, she suffers with dizziness, a symptom not present before delivery; although an aminoglycoside was used in her management, blood levels were always within the therapeutic range. One patient with eclampsia suffered an intracranial haemorrhage secondary to hypertension; this was demonstrated by computerised tomography before admission to ICU. She had a significant neurological deficit at discharge. Another patient required a laryngectomy for a malignant laryngeal tumour, and is still alive at the time of writing.

Two patients died from progressive respiratory failure following ARDS.

## Discussion

The incidences of potentially life-threatening pregnancy-associated emergencies are well documented, and the mortality rates that result from these emergencies are well recognised and investigated;[2] however, the incidence of 'near misses' is much more difficult to elucidate. Analysis of the true incidence is complicated by the variety of policies for intensive management of obstetric emergencies, dictated often by available facilities. Some units may admit all 'at risk' patients to a high dependency area, and reserve ICU admission for those patients in need of ventilatory support. The 'near misses' may become impossible to distinguish from the 'at risk' population if facilities exist to provide mechanical ventilation within an internal high dependency area. The decision to admit a patient to ICU is largely at the discretion of the on-call anaesthetists in this hospital; the facilities are used for mechanical ventilation or intensive monitoring of the critically ill or unstable patient. The less unstable 'at risk' patients may be managed on the labour suite or appropriate wards.

No previous studies of this type seem to have been undertaken, and we were uncertain about the best method of classification of causes of admission. We elected to use the classification system of the United Kingdom maternal mortality studies,[2] on the premise that an ICU admission in our hospital was associated with a life-threatening incident. The proportion of patients in our morbidity study is similar in some groups to the incidence of maternal mortality; however, a number of the causes of death in the mortality reports would preclude the patient reaching an ICU. The incidence of hypertensive diseases in pregnancy was very high in our study, probably because a number of patients in this group were admitted for observation and stabilisation after operative delivery.

It appears from our data that approximately one ICU admission may be expected for every 1000 obstetric deliveries. The majority of patients are young and healthy before admission, and rapid recovery may be expected after correction of the acute physiological insult. This principle is reflected in the high proportion of patients admitted for a period of less than 48 hours, or who required mechanical ventilation for overnight support only. Other studies have shown that the frequency of the need for intervention in patients admitted for observation only may be as low as 14%, but that those who do require intervention are subject to a high risk of mortality and morbidity.[3,4]

## References

1. Crawford JS, Opit LJ. A survey of the anaesthetic services to obstetrics in the Birmingham Hospital Region. A summary. *Anaesthesia* 1976; **31:** 56–9.
2. Turnbull AC, Tindall VR, Robson G, Dawson IMP, Cloake EP, Ashley JSA. *Report on confidential enquiries into maternal deaths in England and Wales 1979–1981.* London: HMSO, 1986.
3. Knaus WA, Wagner DP, Draper EA, Lawrence DE, Zimmerman JE. The range of intensive care services today. *Journal of the American Medical Association* 1981; **246:** 2711–6.
4. Thibault GE, Mulley AG, Barnett GO, Goldstein RL, Reder VA, Sherman EL, Skinner ER. Medical intensive care: indications, interventions, and outcomes. *New England Journal of Medicine* 1980; **302:** 938–42.

*Anaesthesia,* 1989, Volume 44, pages 585–587

CASE REPORT

# Recurrent anaphylactoid reaction during Caesarean section

I. J. B. JACKSON, M. R. BRYSON, S. McPHAIL AND B. B. BHALA

## Summary

*A 28-year-old woman presented for emergency Caesarean section at 31 weeks' gestation with deranged liver function and a history of recurrent anaphylactoid reactions during previous pregnancy-related anaesthetics. The anaesthetic management and outcome of this case is presented.*

## Key words

*Allergy*; anaphylaxis.
*Anaesthesia*; obstetric.

The mechanism of the anaphylactoid response to intravenous agents is the subject of many papers.[1-3] Management of a patient with a history of hypersensitivity reaction to intravenous drugs is still the subject of debate.[4] Many anaesthetists have adopted a technique utilising $H_1$ and $H_2$ receptor antagonists,[3,4] combined with the avoidance of agents known to cause histamine release. The adoption of alternative anaesthetic techniques such as regional blockade is another solution. This case report describes an anaesthetic given for Caesarean section where a hypersensitivity reaction occurred despite the use of a combination of $H_1$ and $H_2$ receptor antagonists and a regional technique.

## Case history

The patient was a 28-year-old woman in her fourth pregnancy who had one surviving child. Her first pregnancy resulted in a ruptured ectopic that required salpingectomy and a 7 unit blood transfusion. There was no evidence of an allergic response during this anaesthetic. She required emergency delivery by Caesarean section at 30 weeks' gestation because of placental abruption in her second pregnancy. She developed bronchospasm, cyanosis, tachycardia and oedema that involved the face and upper airway immediately after delivery of the baby. The reaction responded to general measures but the patient was admitted to the intensive care unit for 48 hours and required a period of artificial ventilation. The third pregnancy required termination at 23 weeks by hysterotomy, because of liver and renal compromise thought to be a sequela of severe pre-eclampsia but which in retrospect might have been the result of fatty liver of pregnancy. She developed a similar allergic response after evacuation of the uterus during this anaesthetic. Subsequent skin testing with the anaesthetic agents used proved negative, but it was noted she was atopic, required antihistamines to control her hay fever and gave a history of developing facial oedema on eating eggs.

Antenatal review was undertaken every 2 weeks in the consultant unit because of her poor obstetric record. Anaesthetic advice was sought because of the past history of reactions during anaesthesia, and tests of hepatic, renal and haematological function were performed at each visit to the clinic. Thrombocytopenia, which developed at 24 weeks' gestation responded promptly to treatment with aspirin 150 mg daily. She was admitted to hospital at 31 weeks with a 2-day history of epigastric pain and vomiting; the symptoms were similar to those that occurred in her previous pregnancy. She was apyrexial, dehydrated but not icteric on examination.

Marked tenderness was elicited in the epigastrium but the uterus was nontender, compatible with her dates, and a cardiotocogram was within normal limits. Investigations (Table 1) revealed a leucocytosis and abnormal clotting together with an elevated AST. The clinical picture raised the possibility of fatty liver of pregnancy and it was concluded that prompt delivery was necessary (via Caesarean section in view of her previous uterine surgery) for both maternal and fetal well being.

---

I.J.B. Jackson,* FFARCS, Registrar, M.R. Bryson, FFARCS, Consultant, S. McPhail,† MRCOG, Registrar in Obstetrics, Princess Mary Maternity Hospital, Newcastle Upon Tyne, B.B. Bhala, FFARCS, Consultant, South Shields General Hospital, South Shields, Tyne and Wear.
*Present position: Senior Registrar, Royal Victoria Infirmary, Newcastle Upon Tyne.
†Present position: Research Registrar, Princess Mary Maternity Hospital, Newcastle Upon Tyne.
Accepted 10 January 1989.

0003–2409/89/070585+03 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Results of initial investigations.

| | |
|---|---|
| *Electrolytes and liver function* | |
| Sodium | 136 mmol/litre |
| Potassium | 3.7 mmol/litre |
| Chloride | 107.0 mmol/litre |
| Bicarbonate | 18.6 mmol/litre |
| Urea | 3.5 mmol/litre |
| Creatinine | 73.0 mol/litre |
| Bilirubin | 11.0 mol/litre |
| Alkaline phosphatase | 151.0 units/litre |
| Aspartate aminotransferase (AST) | 104.0 units/litre |
| *Haematology* | |
| Hb | 11.2 g/dlitre |
| White cell count | $16.6 \times 10^9$/litre |
| Platelets | $160 \times 10^9$/litre |
| *Clotting studies* | |
| | Patient (control) |
| Prothrombin time, seconds | 15 (14) |
| Partial thromboplastin time (PTT), seconds | 133 (50) |
| Thrombin time, seconds | 10 (11) |

An attempt was made to improve her clotting diathesis before Caesarean section. An intravenous line was established and chlorpheniramine 10 mg and ranitidine 50 mg were given intravenously. The patient and fetus were continuously monitored whilst 2 units of fresh frozen plasma were given. A further clotting screen was then performed and in view of the marked improvement it was decided to proceed. The choice of anaesthetic technique was difficult. A regional technique was favoured because of the previous problems and the possible association with general anaesthetic agents. The abnormal clotting ruled out an epidural so we used spinal anaesthesia instead.

The patient was positioned sitting on the theatre table and an ECG monitor and Datascope noninvasive blood pressure monitor attached. Thirty millilitres of 0.3 molar citrate was administered orally. Her circulation was preloaded with 1000 ml of warmed crystalloid solution, while the spinal was established. Chlorhexidine in alcohol was used for skin preparation. Dural puncture was performed using a 26-gauge spinal needle and 2.5 ml 0.5% heavy bupivacaine injected. She was then placed in the supine position with lateral tilt and oxygen administered via a 40% Ventimask. Arterial blood pressure was monitored every minute during onset of the block and every 3 minutes thereafter. A brief episode of hypotension occurred after 5 minutes which responded to ephedrine 3 mg. A bilateral $T_5$ block was achieved by 15 minutes, during which time a further 500 ml of warmed crystalloid was infused. The operation was then allowed to commence.

A live female infant was delivered 15 minutes after the start of the procedure and 40 minutes after the induction of the spinal. The patient complained of some difficulty in breathing immediately after delivery of the infant and placenta and in the absence of any drug administration. She developed marked peri-orbital oedema, plus oedema of her tongue. Mild stridor and bronchospasm were also present. Her arterial blood pressure remained stable but she developed a marked tachycardia, the pulse rate increased from 90 to 135 beats/minute. Hydrocortisone 200 mg and chlorpheniramine 10 mg were administered intravenously and oxygen therapy continued. There was no progression of her symptoms after this. No further measures were taken other than continued reassurance of the patient. The procedure was completed and the patient intensively monitored on the labour ward overnight.

**Table 2.** Complement and IgE levels.

| Test level | Reference range |
|---|---|
| $C_3$ 0.9 g/litre | 0.65– 1.7 |
| $C_4$ 0.2 g/litre | 0.1 – 0.42 |
| IgE 141 IU | 10.0 –150.0 |

The tachycardia settled to normal over the subsequent 6 hours and the oedema resolved during the 24 hours after delivery. No other problems were encountered. She made good progress, though her PTT took 48 hours to return to normal and her AST only slowly returned to normal over the subsequent 2 weeks. Blood samples were obtained during the reaction and sent for evaluation of $C_3$, $C_4$ and IgE levels (Table 2). These revealed a mildly elevated IgE level consistent with atopy and no change in complement levels. Further investigation has revealed that the patient has weakly positive antinuclear antibodies, but strongly positive DNA binding at a level usually seen in active systemic lupus erythematosus. The lupus anticoagulant was not present, anti Ro and La antibodies were negative and the patient has no clinical signs of the condition. Skin testing to bupivacaine was negative.

## Discussion

This patient presented a variety of problems. The link between the previous reactions and anaesthetic agents seemed strong but unconfirmed and led to the choice of anaesthetic given on this occasion. The histamine antagonists were given because of the need to correct the clotting diathesis with fresh frozen plasma and also to provide prophylactic cover for any drugs that may have been required during the procedure. The use of $H_1$ and $H_2$ receptor antagonists in combination with drugs thought to be clean from histamine release has been recommended for maximum safety when a patient with such a history is given an anaesthetic.[4] Regional anaesthetic techniques are also believed to be safe and the use of both principles was considered desirable in this case.

The patient gave a history of uneventful general anaesthesia for an ectopic pregnancy during which she was exposed to thiopentone, suxamethonium, fentanyl and alcuronium. The first reaction occurred during anaesthesia that involved methohexitone, pancuronium and phenoperidine. The choice of agents on the second occasion was modified to those thought to cause minimal histamine release and included etomidate, atracurium, alfentanil and metoclopramide. Skin testing to all these agents has subsequently been shown to be negative.

Each reaction has immediately followed the delivery of the baby. No drugs were administered on this occasion during the 30 minutes before the reaction, and maternal sensitisation to amniotic fluid seems the most probable explanation. There is no immunological evidence to suggest the patient is suffering from hereditary angioneurotic oedema and the elevated IgE is consistent with the patient's atopic history. Prostaglandin release may have played a role since therapeutic doses of aspirin had been stopped 2 days before admission.

Acute fatty liver of pregnancy was a possible antenatal diagnosis and because of the associated high maternal and fetal mortality[5] delivery was expedited, but in the absence of histological evidence this diagnosis cannot be confirmed. Strong DNA binding, in the range normally found in active systemic lupus erythematosus, is in keeping with the patient's poor obstetric record.[6] This auto-immune disease may be exacerbated by pregnancy but there are no reports that anaphylactic reactions are more common in these patients.

This patient was sterilised at the time of Caesarean section and although all problems to date have been associated with pregnancy, her response to other surgical trauma remains unknown. She has been counselled in view of this on the possibility of future problems during surgery and anaesthesia. The patient still developed a potentially life threatening reaction despite our efforts. Investigation has failed to determine a specific cause. This serves to demonstrate that even with careful preparation of these patients problems can still be encountered.

## References

1. Watkins J, Thornton JA, Clarke RSJ. Adverse reactions to i.v. agents. *British Journal of Anaesthesia* 1979; **51:** 469.
2. Bird AG. 'Allergic' drug reactions during anaesthesia. *Adverse Drug Reaction Bulletin*. February 1985, No 110. 408–11.
3. Watkins J, Wild G, Clarke RSJ. Allergy, plasma IgE level and anaphylactoid response: a hypothesis. *Anaesthesia* 1985; **40:** 362–5.
4. Histamine and antihistamine in anaesthesia and surgery. Symposium held 3–5 June, 1981 in Munich. *Klinische Wochenschrift* 1982; **60:** 871–1062.
5. Burroughs, AK, Seong NH, Dojcinov DM, Scheuer PJ, Sherlock SVP. Idiopathic acute fatty liver of pregnancy in 12 patients. *Quarterly Journal of Medicine* 1982; **51:** 481–97.
6. Nicholas NS. Rheumatic diseases in pregnancy. *British Journal of Hospital Medicine* 1988; **39:** 50–3.

*Anaesthesia*, 1989, Volume 44, pages 588–589

CASE REPORT

# Giant false aneurysm of the subclavian artery

## An unusual complication of internal jugular venous cannulation

S. P. J. HUDDY, A. McEWAN, J. SABBAT AND D. J. PARKER

### Summary

*A false aneurysm with a diameter of 15 cm developed in the wall of the subclavian artery after attempted internal jugular cannulation. This potentially lethal complication, its diagnosis and treatment are described.*

### Key words

*Veins*; internal jugular, cannulation.
*Complications*; false aneurysm.

Central venous cannulation is a procedure which is performed commonly. Borja[1] reported a complication rate of between 0.4% and 9.9% and identified 15 deaths due to the procedure in the English literature to 1972. Cannulation of the internal jugular vein, described first by Hermosura *et al.*[2] is thought to be safer than subclavian vein cannulation.[3] In this report, we describe a life-threatening complication of attempted right internal jugular venous cannulation.

### Case history

A 36-year-old caucasian male was admitted to another hospital with grand mal fits. His condition deteriorated over the next few days and he became septic. An attempt was made to cannulate the right internal jugular vein by a high approach using a 16-gauge 'Wallace' cannula. This resulted in an arterial puncture. The procedure was abandoned and a cannula was inserted successfully on the left side. An X ray taken later showed some widening of the upper mediastinum but was thought to be normal in other respects. An echocardiogram was performed which was reported to show a little pericardial fluid but no evidence of aortic dissection. It was thought that the mediastinal widening represented a haematoma. The patient was discharged home after recovery from his presenting condition and arrangements were made for him to be followed up in the outpatient department.

The patient presented in the casualty department 3 weeks after the attempted jugular venous cannulation. He complained of progressive shortness of breath (which now affected him at rest), a hoarse voice and recurrent fevers. On examination, he was pale and tachypnoeic. He had a hoarse voice and mild stridor was present. The physical signs of a right pleural effusion were detected. A mass was palpable in the right supraclavicular fossa with a thrill and a loud bruit on auscultation. Peripheral pulses were present and equal on both sides. The chest X ray at this time is shown in Figure 1. He was transferred to this hospital and

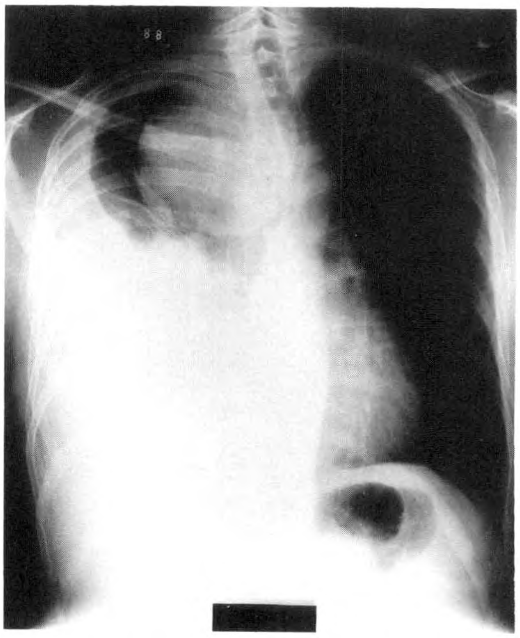


**Fig. 1.** Chest X ray showing a large right haemothorax and a false aneurysm of the right subclavian artery, which displaces the trachea to the left.

---

S.P.J. Huddy, MChir, FRCS, Surgical Registrar, A. McEwan, MB, ChB, Anaesthetic Registrar, J. Sabbat, MB, BS, Cardiology SHO, D.J. Parker, FRCS, FRCP, Consultant Cardiac Surgeon, South West Thames Regional Cardiothoracic Unit, St George's Hospital, Blackshaw Road, London SW17 0QT.

Accepted 21 December 1988.

0003–2409/89/070588+02 $03.00/0

© 1989 The Association of Anaesthetists of Gt Britain and Ireland

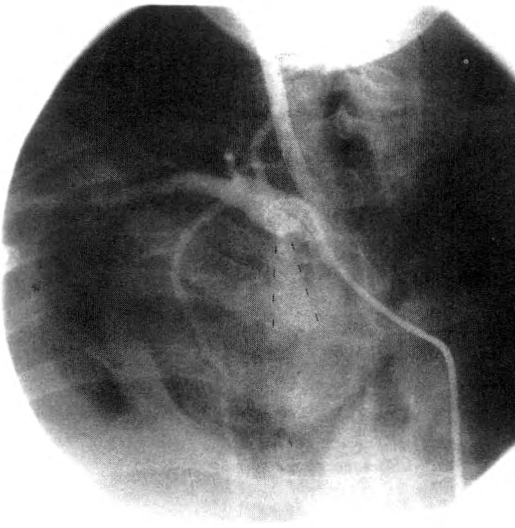


**Fig. 2.** A still frame from an angiogram which demonstrates a false aneurysm of the right subclavian artery. The fan-shaped jet of blood leaking from the artery is indicated with a dashed outline.

underwent aortography via a femoral approach. A representative frame from the cinematographic film is shown in Figure 2. This demonstrates a false aneurysm which arises from the first part of the subclavian artery; a significant fan-shaped jet of contrast entered the aneurysm. He was taken to theatre and the aneurysm was repaired through a mediastinotomy extended laterally above the right clavicle. The aneurysm was found to arise from the inferior aspect of the first part of the subclavian artery mid-way between the origin of the vertebral and right common carotid arteries. The surrounding area was indurated and recognition of nerve tissue was not possible. There was a 3-mm laceration in the inferior aspect of the subclavian artery and blood leaked through this into the false aneurysm. The artery was controlled with tapes, the defect sutured and a saphenous vein patch inserted. Approximately one litre of blood clot was removed from the right pleural space. He made a satisfactory postoperative recovery. On review at 3 months, he remained hoarse, with a right recurrent laryngeal nerve palsy and Horner's syndrome.

## Discussion

Many different complications of internal jugular venous cannulation have been reported and these have been reviewed extensively by Sladen[4] and by Kaye and Smith.[5] The most common complications are infection, haemorrhage, pneumothorax, air embolism and arterial puncture. The incidence of arterial puncture during internal jugular vein cannulation has been reported to be 4.2% by Schwartz *et al.*[6] but this is seldom of clinical significance. Complications which have been reported after inadvertent arterial puncture include laceration of the artery, haemothorax and arteriovenous fistula formation.[4]

The carotid artery is the vessel damaged most commonly. Haemorrhage from the carotid artery can be controlled usually by digital pressure unless the arterial puncture is not recognised and a large bore cannula introduced.[6] Subclavian artery puncture may result in the development of an extensive haematoma especially if the pleura is also damaged.[4] A chest X ray should be performed after central venous cannulation and examined to detect a haematoma. In our case, the mediastinum was noted to be widened but echocardiography demonstrated no abnormality. Angiography at this stage might have allowed an earlier diagnosis of the false aneurysm and prompt repair, which would have been easier with a smaller aneurysm and before the surrounding area became indurated.

Robinson *et al.*[7] have suggested previously that it should be routine after a difficult cannulation for auscultation to be performed on the neck within 2 weeks in order to detect arteriovenous fistulae. This manouevre might have helped to identify the complication which we report here although not all aneurysms are associated with a bruit.

## References

1. Borja AR. Current status of infraclavicular subclavian vein catheterization: review of the English literature. *Annals of Thoracic Surgery* 1972; **13:** 615–24.
2. Hermosura B, Vanags L, Dickey MW. Measurement of pressure during intravenous therapy. *Journal of the American Medical Association* 1966; **195:** 321.
3. Modell JH. Indications, management, and complications of percutaneous subclavian catheters. *Archives of Surgery* 1978; **113:** 1425.
4. Sladen A. Complications of invasive hemodynamic monitoring in the intensive care unit. *Current Problems in Surgery* 1988; **25:** 75–145.
5. Kaye CG, Smith DR. Complications of central venous cannulation. Trauma, infection, and thrombosis. *British Medical Journal* 1988; **297:** 572–3.
6. Schwartz AJ, Jobes DR, Greenhow DE, Stephenson LW, Ellison N. Carotid artery puncture with internal jugular cannulation. *Anesthesiology* 1979; **51:** S160.
7. Robinson PN, Jewkes DA, Kendall B. Vertebrovertebral arteriovenous fistula. A complication of internal jugular catheterisation. *Anaesthesia* 1984; **39:** 46–7.

*Anaesthesia,* 1989, Volume 44, pages 590–591

# Forum

## Sodium bicarbonate as a single dose antacid in obstetric anaesthesia

H.M.L. Mathews, FFARCS, Senior Registrar, J. Moore, MD, PhD, FFARCS, Consultant, Department of Anaesthetics, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL.

### Summary

*Gastric pH and volumes were measured in 84 women who had general anaesthesia for emergency Caesarean section. Forty-eight received only 20 ml 8.4% sodium bicarbonate immediately before induction of anaesthesia and 36 ranitidine 150 mg 6-hourly during labour in combination with* $NaHCO_3$*. Gastric pH was less than 2.5 in four women who received only bicarbonate. All aspirates from the ranitidine plus bicarbonate group had a pH greater than 2.5. Mean volumes of gastric content aspirated were 87 (SD 87.4) and 60 (SD 46.3) ml for the bicarbonate alone and bicarbonate plus rantidine series respectively. These differences were not significant. Twenty millilitres of 8.4%* $NaHCO_3$ *cannot be recommended as a single dose antacid for emergency Caesarean section. Ranitidine plus bicarbonate is considered a reliable antacid regimen to ensure elevation of gastric pH to safe levels.*

### Key words

*Gastrointestinal tract*; stomach pH, volume.
*Histamine*; $H_2$ receptor antagonist, ranitidine.

Ranitidine 150 mg given orally every 6 hours during labour does not raise the pH of gastric contents above 2.5 in all patients.[1] However, the addition of 20 ml 8.4% sodium bicarbonate orally immediately before general anaesthesia did ensure that gastric pH was raised to safe levels in 100% of cases.[2] Failure of ranitidine alone was mainly due to its single administration in emergency situations where anaesthesia was required within an interval of 2 hours. This was an inadequate time period to empty existing stomach acid and to achieve therapeutic plasma levels of the $H_2$ blocker. However, the administration of sodium bicarbonate in such situations ensured that no patient had gastric contents with pH less than 2.5. These findings prompted further investigation of the efficacy of 8.4% sodium bicarbonate alone as a single pre-anaesthetic treatment in the elevation of gastric pH, as well as a further assessment of the value of ranitidine to reduce gastric volumes.

### *Method*

The study had local Ethics Research Committee approval and all women gave verbal consent. Patients admitted to the delivery ward were allocated, each month, to receive either ranitidine 150 mg orally, 6-hourly or no regular antacid therapy. The method of allocation to the two groups, though not ideal, was used to facilitate administration of either therapy by the midwives. All patients who required emergency general anaesthesia received 20 ml 8.4% $NaHCO_3$ immediately before pre-oxygenation. They were anaesthetised by a technique that involved pre-oxygenation, rapid intravenous induction, application of cricoid pressure and muscle relaxation followed by tracheal intubation. A lightly lubricated No. 18 Salem sump tube was introduced into the stomach through a 8.0 uncuffed tracheal tube placed in the oesophagus, when anaesthesia was established. Ten millilitres (sample A1) of gastric contents were aspirated as soon as possible after induction. The remainder of the stomach contents was aspirated just before termination of the anaesthetic and the volume measured (sample A2). pH was measured with a Corning 113 pH meter and microelectrode. Times from administration of $NaHCO_3$ to aspiration of samples A1 and A2 were noted as well as those patients who received narcotics.

Those mothers not given rantidine received a further 20 ml $NaHCO_3$ before withdrawal of the Salem sump tube to ensure a high gastric pH during emergence, since sodium bicarbonate has been shown to have a brief neutralising action.[3]

The results are presented as mean (SD) and differences were compared statistically using the unpaired Student's *t*-tests.

### *Results*

Eighty-four patients who required emergency Caesarean section were included; 48 were given $NaHCO_3$ alone and 36 received ranitidine plus $NaHCO_3$. The times from $NaHCO_3$ administration to gastric aspiration and the pH of the samples A1 and A2 are shown in Table 1. Four of A1 samples and two of the two A2 samples after bicarbonate-only treatment had pH below 2.5 and were taken approximately 15 and 40 minutes respectively after the antacid treatment. All aspirates from the ranitidine plus bicarbonate series had a pH greater than 2.5. None of the differences in pH was statistically significant.

---

Accepted 28 November 1988.

0003–2409/89/070590+16 $03.00/0 © 1989 The Association of Anaesthetists of Gt Britain and Ireland

**Table 1.** Mean (SD) times from bicarbonate treatment to gastric aspiration and mean pH (SD) with range of samples A1 and A2.

| | Gastric aspirates | | | |
|---|---|---|---|---|
| | A1 | | A2 | |
| | Time from $NaHCO_3$ (minutes) | pH (range) | Time from $NAHCO_3$ (minutes) | pH (range) |
| $NaHCO_3$ | 14 (6.2) | 7.7 (2.25)<br>(0.9–9.7) | 40 (11.4) | 7.3 (2.41)<br>(0.9–9.8) |
| Ranitidine + $NaHCO_3$ | 12 (3.4) | 8.2 (0.96)<br>(5.8–10.0) | 42 (13.4) | 8.1 (1.01)<br>(6.0–10.0) |

**Table 2.** Mean (SD) with range of gastric volumes.

| | Narcotics (ml) | No narcotics (ml) |
|---|---|---|
| $NaHCO_3$ | $n=25$<br>112 (88.3)<br>(18–300) | $n=23$<br>61 (79.7)<br>(12–340) |
| Ranitidine + $NaHCO_3$ | $n=19$<br>75 (54.4)<br>(14–196) | $n=17$<br>43 (27.6)<br>(5–123) |

The mean volumes of gastric content aspirated were 87 (SD 87.4) and 60 (SD 46.3) ml for the bicarbonate alone and bicarbonate plus ranitidine series respectively. These differences were not statistically significant. Nine patients in the bicarbonate-only and five in the bicarbonate-plus ranitidine groups had gastric aspirates less than 25 ml. Table 2 shows the volumes related to the prior treatment with narcotic analgesics. The gastric volumes were significantly less after either antacid treatment when no narcotics were given ($p < 0.05$).

## *Discussion*

It was hoped that the numbers in this study would have been greater. However, an incidence of 9% failure to achieve elevation of gastric pH above 2.5 in the bicarbonate-only group was thought unacceptable and it was considered inadvisable to continue with this study. Lim and Tan[4] treated 55 emergency obstetric patients with an immediate pre-anaesthetic dose of 20 ml 8.4% $NaHCO_3$ and found that the lowest intragastric pH was 6.84. Our findings unfortunately disagree with this study and we therefore cannot recommend 20 ml 8.4% $NaHCO_3$ as a single dose antacid for emergency Caesarean section in labouring patients. Perhaps because of the small numbers in the study ranitidine did not significantly decrease the volume of gastric contents in labouring patients. Indeed, less than 20% of patients in both groups had gastric volumes less than 25 ml, the figure suggested by Roberts and Shirley[5] for the patient at risk of gastric content aspiration. Previous work had shown that ranitidine decreased the volume of gastric contents in labour when compared with patients who received regular 2-hourly administration of mist. magnesium trisilicate BPC,[1] but in this study patients received only one pre-anaesthetic dose of $NaHCO_3$. This may explain why gastric contents were not significantly less with ranitidine in our study. Gastric volumes were significantly less in patients who did not receive narcotics despite the small numbers; this emphasises the well known effect of narcotics on gastric emptying.

In conclusion, ranitidine 150 mg 6-hourly during labour in combination with a saline antacid immediately before general anaesthesia is considered a reliable antacid regimen to ensure safe elevation of gastric pH.

## *Acknowledgments*

The authors thank the obstetricians and nursing staff of Jubilee Maternity Hospital, Belfast and anaesthetic staff of Belfast City Hospital and the Ulster Hospital, Dundonald for their help in this study.

## *References*

1. McAuley DM, Moore J, Dundee JW, McCaughey W. Oral ranitidine in labour. *Anaesthesia* 1984; **39:** 433–8.
2. Mathews HML, Wilson CM, Thompson EM, Moore J. Combination treatment with rantidine and sodium bicarbonate prior to obstetric anaesthesia. *Anaesthesia* 1986; **41:** 1202–6.
3. Lahiri SK, Thomas TA, Hodgson RMH. Single-dose antacid therapy for the prevention of Mendelson's syndrome. *British Journal of Anaesthesia* 1973; **45:** 1143–6.
4. Lim HS, Tan PL. Sodium bicarbonate injection, U.S.P. as an oral antacid for emergency Caesarean Section patients. *Anesthesiology* 1981; **55:** A339.
5. Roberts RB, Shirley MA. Reducing the risk of acid aspiration during Caesarean section. *Anesthesia and Analgesia* 1974; **53:** 859–68.

---

*Anaesthesia,* 1989, Volume 44, pages 591–593

# The effect of $H_2$ antagonists on duration of action of suxamethonium in the parturient

D. G. Bogod,* FFARCS, Senior Medical and Health Officer, Honorary Clinical Lecturer, T. E. Oh, FFARACS, Professor, Chinese University of Hong Kong, Department of Anaesthesia and Intensive Care, Prince of Wales Hospital, Shatin, New Territories, Hong Kong.

## Summary

*Fifteen patients who underwent elective Caesarean section were given sodium citrate, either alone or combined with oral cimetidine or ranitidine, as antacid premedication. No significant differences in time to 25 or 50% recovery of the first twitch of a train-of-four after administration of suxamethonium were found between any of the groups. It is concluded that $H_2$-antagonists do not significantly affect the duration of action of suxamethonium in parturients, in contrast to the findings of a study in nonpregnant patients.*

## Key words

*Histamine*; $H_2$-receptor antagonist, cimetidine, ranitidine.
*Neuromuscular relaxants*; suxamethonium.

Suxamethonium is used routinely during general anaesthesia for Caesarean section to provide rapid intubating conditions after induction in order to reduce the risk of acid aspiration. A reduction in plasma cholinesterase activity is a consistent finding in late pregnancy.[1] This does not usually result in prolongation of suxamethonium action,[2] but it may unmask patients who are heterozygous for an atypical cholinesterase.

The oral administration of $H_2$-receptor antagonists as premedication before Caesarean section is gaining popularity. A regimen that comprises cimetidine 300 mg or ranitidine 150 mg administered the night before and 2 hours prior to surgery, combined with a suitable antacid such as sodium citrate, results usually in a small volume of gastric contents with a pH greater than 2.5.[3-5] A recent study[6] has shown that the duration of action of suxamethonium is increased by a factor of 2–2.5 in nonpregnant patients premedicated with cimetidine.[6] This may be due to direct inhibition of liver enzymes and reduction in hepatic blood flow associated with the use of cimetidine, a property not shared by the second-generation $H_2$ antagonist ranitidine.[7,8]

The purpose of the present study was to determine whether premedication with cimetidine or ranitidine affected the duration of action of suxamethonium significantly in full-term parturients who underwent Caesarean section.

### *Methods*

Fifteen patients who underwent elective Caesarean section under general anaesthesia at term were included in the trial. The study was approved by the University's Ethics Committee and all patients gave informed consent. None of the subjects had a personal or family history suggestive of cholinesterase deficiency. Patients were allocated randomly into one of three groups: Group 1 (control)—no $H_2$ antagonist; Group 2 (cimetidine)—oral cimetidine 300 mg was administered the previous night and again 2 hours preoperatively; Group 3 (ranitidine)—oral ranitidine 150 mg was administered the previous night and again 2 hours preoperatively. All patients were fasted for at least 6 hours and received oral sodium citrate 30 ml one hour pre-operatively. All anaesthetics were administered by the same anaesthetist.

The electrodes of a Datex NMT-100 Relaxograph were applied before induction to the noninfusion arm of the patient in order to stimulate the ulnar nerve and record the response from the *adductor pollicis brevis* muscle.

After pre-oxygenation, cricoid pressure was applied by a trained assistant before administration of a sleep dose of thiopentone. The automatic calibration sequence of the Relaxograph was initiated immediately, and after confirmation of the setting of a 100% reference level, suxamethonium 1.5 mg/kg was administered. Tracheal intubation was performed when clinical neuromuscular block was apparent. Anaesthesia was maintained with 50% nitrous oxide and 1% enflurane in oxygen, using a tidal volume of 10 ml/kg and a respiratory rate of 10 breaths/minute.

Train-of-four supramaximal stimulation was applied automatically by the Relaxograph at 20-second intervals and the ratio of the first twitch response to the reference value ($T_1$%) was displayed and recorded. The times taken from administration of suxamethonium to $T_1$ values of 25% and 50% were measured. A nondepolarising muscle relaxant was administered at 50% recovery. The block was reversed with atropine and neostigmine at the end of the procedure when at least three twitch responses were apparent. Full reversal, indicated by a $T_4$:$T_1$ ratio of at least 80%, was seen in all patients within 6 minutes.

The results were analysed by one-way analysis of variance, and a value of $p < 0.05$ was regarded as statistically significant.

### *Results*

There were five patients in each group; all were of Chinese origin, and were resident in Hong Kong. Their weights ranged from 42 to 96 kg (mean 61 kg), and there were no significant weight differences between the groups (Table 1).

The time taken in seconds to reach 25% and 50% recovery for each patient is shown graphically in Figure 1, with the means and standard deviations in Table 1. There were no statistically significant differences between any of the groups.

### *Discussion*

The use of $H_2$-antagonists in combination with a nonparticulate antacid such as sodium citrate has been recommended to ensure high gastric pH and low volume of gastric contents in parturients.[4,5] Cimetidine is known to interfere with the metabolism of other drugs by an effect on oxidative metabolism,[7,8] and this has been shown to decrease bupivacaine clearance significantly in volunteers.[9] The same study showed that ranitidine did not share this property.

A recent study by Kambam *et al.*[6] in nonpregnant patients showed that the time to 50% recovery of first twitch response was prolonged from a mean (SEM) time of 8.6 (0.76) minutes in a control group, to 20.3 (4.25) minutes in patients who had received two oral doses of cimetidine 300 mg. It was postulated that this may be related to the effect of cimetidine upon hepatic metabolism, and the authors recommended further investigation to elucidate the exact mechanism involved.

---

*Present address: Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW.
Accepted 8 February 1989.

**Table 1.** Weight of patients and time to 25% and 50% recovery of first twitch after administration of suxamethonium.

| | Weight (kg) | | | 25% recovery time (second) | | | 50% recovery time (second) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Control | Cimetidine | Ranitidine | Control | Cimetidine | Ranitidine | Control | Cimetidine | Ranitidine |
| | 57 | 58 | 56 | 440 | 540 | 380 | 540 | 600 | 440 |
| | 60 | 50 | 53 | 560 | 540 | 500 | 680 | 600 | 580 |
| | 64 | 42 | 70 | 600 | 520 | 620 | 700 | 640 | 660 |
| | 60 | 90 | 96 | 640 | 540 | 640 | 740 | 660 | 680 |
| | 72 | 45 | 42 | 660 | 640 | 640 | 760 | 740 | 700 |
| Mean | 62.6 | 57 | 63.4 | 580 | 556 | 556 | 684 | 648 | 612 |
| SD | 5.8 | 19.4 | 20.8 | 87 | 48 | 114 | 87 | 58 | 106 |

The present study set out to determine whether this effect could be reproduced in full-term parturients. Kambam's results were used as a guide to the variability of response to suxamethonium, and power analysis suggested that the presence of five patients in each group would result in an 80% power to detect a 50% change in suxamethonium response with 95% confidence intervals.

Patients in late pregnancy are known to have concentrations of plasma cholinesterase that are reduced by 30% from nonpregnant values.[1] Thus it might be supposed that further inhibition of suxamethonium metabolism would have a greater clinical effect on duration of action. This has not been demonstrated. The times to 50% recovery in all groups in the present study are slightly longer than in Kambam's control group, although this reaches statistical significance only in Group 1 (control) ($t = 2.366$, $p = 0.034$). The times to 25 and 50% recovery of the cimetidine and ranitidine groups in the present study are slightly less than the control group (not statistically significant), in marked contrast to Kambam's study.

The reason for the difference in results between these two studies requires further elucidation, particularly because of the potential clinical importance of prolongation of action of suxamethonium by cimetidine. The plasma concentrations of cimetidine and ranitidine exhibit inter-individual variability in critically ill patients[10,11] and this phenomenon may occur in our pregnant Chinese patients. A further study that includes pharmacokinetic analysis of both drugs and assay of cholinesterase concentrations is indicated. Meanwhile, the present study has shown that, in a population of full-term Chinese parturients, premedication with $H_2$-antagonists has no significant effect on the duration of action of suxamethonium.

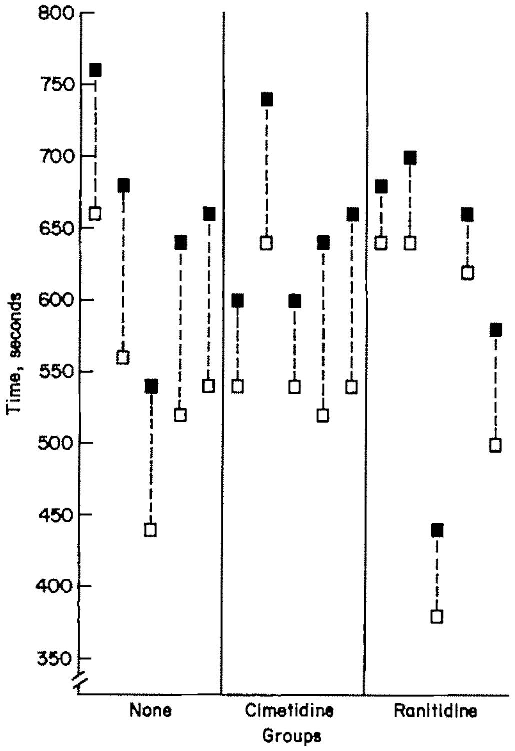


**Fig. 1.** Time taken for each patient to recover neuromuscular function after administration of suxamethonium. ■, 50% recovery of T1; □, 25% recovery of T1.

## *Acknowledgments*

We are grateful to the obstetric and midwifery staff of ward 5E of the Prince of Wales Hospital for their help with this study.

## *References*

1. Shnider SM. Serum cholinesterase activity during pregnancy, labor and the puerperium. *Anesthesiology* 1965; **26:** 335–9.
2. Blitt CD, Petty WC, Alberternst EE, Wright BJ. Correlation of plasma cholinesterase activity and duration of action of succinylcholine during pregnancy. *Anesthesia and Analgesia* 1977; **56:** 78–83.
3. Hodgkinson R, Glassenberg R, Joyce TH, Coombs DW, Ostheimer GW, Gibbs CP. Comparison of cimetidine (Tagamet®) with antacid for safety and effectiveness in reducing gastric acidity before elective cesarean section. *Anesthesiology* 1983; **59:** 86–90.
4. McAuley DM, Moore J, McCaughey W, Donnelly BD, Dundee JW. Ranitidine as an antacid before elective Caesarean section. *Anaesthesia* 1983; **38:** 108–14.
5. Thompson EM, Loughran PG, McAuley DM, Wilson CM, Moore J. Combined treatment with ranitidine and saline antacids prior to obstetric anaesthesia. *Anaesthesia* 1984; **39:** 1086–90.
6. Kambam JR, Dymond R, Krestow M. Effect of cimetidine on duration of action of succinylcholine. *Anesthesia and Analgesia* 1987; **66:** 191–2.
7. Puurunen J, Sotaniemi E, Pelkonen O. Effect of cimetidine on microsomal drug metabolism in man. *European Journal of Clinical Pharmacology* 1980; **18:** 185–7.
8. Feely J, Wilkinson GR, Wood AJJ. Reduction of liver blood flow and propranolol metabolism by cimetidine. *New England Journal of Medicine* 1981; **304:** 692–5.
9. Noble DW, Smith KJ, Dundas CR. Effects of $H_2$ antagonists on the elimination of bupivacaine. *British Journal of Anaesthesia* 1987; **59:** 735–7.
10. Nation RL, Ilett KF, Tjokrosetio R, Oh TE, Cameron P, Thompson W. Pharmacokinetics of cimetidine in critically ill patients. *European Journal of Clinical Pharmacology* 1984; **26:** 341–6.
11. Ilett KF, Nation RL, Tjokrosetio R, Thompson W, Oh TE, Cameron PD. Pharmacokinetics of ranitidine in critically ill patients. *British Journal of Clinical Pharmacology* 1986; **21:** 279–88.

*Anaesthesia,* 1989, Volume 44, pages 594–595

# Assessing collateral circulation in the hand—four methods compared

R. J. Glavin, MB, ChB, FFARCS, Senior Registrar, H. M. Jones, MB, ChB, FFARCS, Registrar, Division of Anaesthesia, Royal Infirmary, Glasgow, G31 3ER.

## Summary

*Four ways to assess the collateral circulation in the hand were compared. No correlation was shown between the Doppler ultrasound method and those that used either the pulse monitor or the Ohmeda Biox 3700 pulse oximeter. The study was unable to confirm suggested benefits of these methods in assessing adequacy of collateral flow in the hands of unconscious patients.*

**Key words**

*Arteries*; Allen's test.
*Equipment*; pulsed oximetry.

Percutaneous cannulation of the radial artery at the wrist is now commonly performed on patients who have major surgery and intensive care. The adequacy of collateral blood flow to the hand via the ulnar artery is routinely assessed prior to cannulation to avoid ischaemia of the hand. A modified version of the test first described by Allen in 1929[1] is the method generally used to assess the presence of ulnar collateral flow. This test requires the cooperation of the patient and is therefore unsuitable for those who are unconscious. However, alternative methods that rely on either a pulse monitor[2,3] or pulse oximeter[4] and that are suitable for use in the unconscious patient are described, but not fully evaluated.

The present study was undertaken to evaluate assessment of the presence of collateral circulation in the hand. Mozersky and his colleagues[5] assessed the circulation to the hand with the Doppler ultrasound and concluded that this method was more useful than the Allen's test. Little and colleagues[6] demonstrated lack of collateral circulation in 6% of hands using the Doppler ultrasound probe but only in 1.2% of hands using the Allen's test. The Doppler ultrasound has therefore been used as a reference method to assess the collateral circulation of the hand by workers such as Kamienski and colleagues.[7] We decided on this basis to use Doppler ultrasound as our reference method. By comparing the modified Allen's test, the pulse monitor and the pulse oximeter with our reference method we could evaluate these three techniques in the assessment of the presence of ulnar collateral flow to the hand.

### *Methods*

The arterial circulation to both hands was assessed in 75 adults who gave their consent. A nondirectional flow probe (BV 102 Vascular Flow Detector, Sonicaid) was used to confirm flow in the radial and ulnar artery. A modified Allen's test[7] was performed. The patient was asked to make a fist; both arteries were occluded for 30 seconds; the patient then extended the fingers, avoiding hyperextension; the ulnar artery pressure was then released and the timing to full palmar blush noted. Full blush within 6 or less seconds was taken as an indication of acceptable collateral flow.[7]

Finger probes from a pulse oximeter (Biox 3700, Ohmeda) and a pulse monitor (Kontron Medical 108) were placed on the index and middle fingers respectively. The saturation and quality of signal from the oximeter were noted and the amplitude of the pulse monitor waveform measured. The ulnar and radial arteries were once more occluded with sufficient force to render a flat tracing on the monitors. This was also maintained for 30 seconds. The saturation and quality of the signal from the oximeter and the amplitude of the pulse monitor waveform were recorded after release of the ulnar artery compression. A decrease in the amplitude of the waveform did not yield useful information, firstly, because the amplitude of a photo-electric plethysmogram, as is used in both these devices, does not indicate the height of arterial pulse waves in a quantitative way[8] and secondly the Biox 3700 automatically produces a signal of maximal amplitude. Persistence of the flat tracing therefore was taken as an indication of lack of ulnar collateral circulation.

### *Results*

We compared the results from the Doppler ultrasound method with the results from each of the three other methods of assessing the collateral circulation in a series of 2 × 2 tables as described by Sackett *et al.*[9] Table 1 compares the incidence of present and absent ulnar artery blood flow using the Doppler probe and the Allen's test.

**Table 1.** Incidence of presence or absence of ulnar artery flow: Allen's test compared with Doppler ultrasound.

| | Doppler ultrasound | | |
|---|---|---|---|
| | Present | Absent | Total |
| Allen's test | | | |
| Present | 125 | 3 | 128 |
| Absent | 18 | 4 | 22 |
| Total | 143 | 7 | 150 |
| Sensitivity | 0.87 | | |
| Specificity | 0.57 | | |
| Positive predictive value | 0.98 | | |
| Negative predictive value | 0.18 | | |

---

Accepted 30 June 1988.

**Table 2.** Incidence of presence or absence of ulnar artery flow: pulse monitor compared with Doppler ultrasound.

| | Doppler ultrasound | | |
|---|---|---|---|
| | Present | Absent | Total |
| Pulse monitor | | | |
| Present | 138 | 7 | 145 |
| Absent | 5 | 0 | 5 |
| Total | 143 | 7 | 150 |
| Sensitivity | 0.97 | | |
| Specificity | 0 | | |
| Positive predictive value | 0.95 | | |
| Negative predictive value | 0 | | |

**Table 3.** Incidence of presence or absence of ulnar artery flow: pulse oximeter compared with Doppler ultrasound.

| | Doppler ultrasound | | |
|---|---|---|---|
| | Present | Absent | Total |
| Pulse oximeter | | | |
| Present | 143 | 7 | 150 |
| Absent | 0 | 0 | 0 |
| Total | 143 | 7 | 150 |
| Sensitivity | 1.0 | | |
| Specificity | 0 | | |
| Positive predictive value | 0.95 | | |
| Negative predictive value | 0 | | |

Table 2 compares the incidence of present and absent ulnar artery blood flow using the Doppler probe and the pulse monitor, and Table 3 compares the incidence of present and absent ulnar artery blood flow using the Doppler probe and the pulse oximeter.

The sensitivity, specificity, positive predictive value and negative predictive value for each method was calculated as described by Sackett.[9] These values for the Allen's test method are listed with Table 1. Values for the same variables are listed for the pulse monitor and pulse oximeter with Tables 2 and 3 respectively.

The prevalence of ulnar artery blood flow is 0.95; i.e. 95% of hands studied have ulnar artery blood flow present.

## *Discussion*

There is a conflict of opinion about the value of assessing the presence of collateral blood flow to the hand prior to percutaneous radial artery cannulation. Some have claimed that it is of no value in the prediction of damage due to ischaemia[10] while others still recommend its use.[5,11]

The Doppler ultrasound probe showed ulnar artery flow in 95% of hands. This compares with the findings of Little[6] who also found adequate ulnar flow in 94% of patients. Table 1 shows that the modified Allen's test has a sensitivity of 87%; that is, it detected ulnar collateral flow in only 87% of the cases in which Doppler had confirmed the presence of an ulnar artery. The modified Allen's test is even poorer at assessing the absence of an ulnar collateral flow; it has a negative predictive value of 0.18. This means that only 18% of those patients in whom an Allen's test showed no ulnar collateral flow will have no ulnar collateral flow as detected by Doppler. If extrapolated to clinical practice then approximately 80% of patients with a positive Allen's test, i.e. no ulnar collateral flow, would be wrongly denied the benefits of arterial cannulation.

It can be seen from Tables 2 and 3 that neither the pulse monitor nor pulse oximeter identified the absence of ulnar collateral flow in those hands where Doppler had demonstrated lack of ulnar flow. The negative predictive values of these methods therefore cannot be calculated, which means that these two methods are of no value in the detection of absent collateral ulnar artery flow.

We cannot, on this evidence, recommend the use of either the pulse monitor or the Ohmeda Biox 3700 pulse oximeter to detect lack of ulnar collateral flow in the unconscious or uncooperative patient.

## *Acknowledgments*

We thank the Recovery Room Nursing Staff for their assistance with this study and Miss Irene Robertson for her secretarial help.

## *References*

1. ALLEN EV. Thrombangitis obliterans; methods of diagnosis of chronic occlusive arterial lesions distal to the wrist with illustrative cases. *American Journal of Medical Science* 1929; **178**; 237–44.
2. BRODSKY JB. A simple method to determine patency of the ulnar artery intraoperatively prior to radial artery cannulation. *Anesthesiology* 1975; **42:** 626–7.
3. DUNCAN PW. An alternative to Allen's test. *Anaesthesia* 1986; **41:** 88.
4. RAJU R. The pulse oximeter and the collateral circulation. *Anaesthesia* 1986; **41:** 783–4.
5. MOZERSKY DJ, BUCKLEY CJ, HAGOOD CO, CAPPS WF, DANNEMILLAR FJ. Ultrasonic evaluation of the palmar circulation: a useful adjunct to radial artery cannulation. *American Journal of Surgery* 1973; **126:** 810–2.
6. LITTLE JM, ZYLSTRA PL, WEST J, MAY J. Circulatory patterns in the normal hand. *British Journal of Surgery* 1973; **60:** 652–5.
7. KAMIENSKI RW, BARNES RW. Critique of the Allen Test for continuity of the palmar arch assessed by Doppler ultrasound. *Surgery Gynecology and Obstetrics* 1976; **142:** 861–4.
8. DORLAS JC, NIJBOER JA. Photo-electric plethysmography as a monitoring device in anaesthesia. *British Journal of Anaesthesia* 1985; **57:** 524–30.
9. SACKETT DL, HAYNES RB, TUGWELL P. *Clinical epidemiology: a basic science for clinical medicine.* Boston, Toronto: Little, Brown, 1985: 66–100.
10. WILKINS RG. Radial artery cannulation and ischaemic damage: a review. *Anaesthesia* 1985; **40:** 896–9.
11. HUSUM B, BERTHELSEN P. Allen's test and systolic arterial pressure in the thumb. *British Journal of Anaesthesia* 1981; **53:** 635–7.

*Anaesthesia*, 1989, Volume 44, pages 596–599

# Volatile agent use: perception and practice
## A survey of agent use over a 3-year period

J. Tarpey, MB, BCh, BAO, Senior House Officer in Anaesthesia and Intensive Care, P. G. Lawler, FRCP, FFARCS, Consultant in Anaesthesia and Intensive Care, Intensive Therapy Unit, South Cleveland Hospital, Middlesbrough, Cleveland TS3 4BW.

### Summary

*We calculated the quantity, as MAC hours and MAC hours anaesthetic, of halothane, enflurane and isoflurane, used in this Health District over a 3-year period. Halothane accounted for 77% of anaesthesia in the first year and for 57% in the final year. Overall usage of volatile agents decreased. Fifteen consultants and 19 senior registrars perceived, in a survey of practice, only a change in relative use of volatile anaesthetic agents with a large swing from halothane to both enflurane and isoflurane. Half the anaesthetists stated that the medicolegal consideration was the prime reason for their change. The perceived total demise of halothane does not appear to have been realised, despite individual anaesthetist's perceptions.*

### Key words

*Anaesthetics, volatile*; halothane, enflurane, isoflurane.

There has been increasing awareness and concern in the recent past about the consequences of repeated halothane anaesthesia. The recent recommendations of the Committee on Safety of Medicines (CSM), published in September 1986,[1] might be liberally interpreted as to preclude the use of halothane should the patient have ever received an anaesthetic in the previous 30 years, i.e. since the introduction of halothane into clinical practice.

Isoflurane was introduced into the UK approximately 3 years ago, sometime prior to the recent resurgence of this concern about halothane. This agent is considerably more expensive than halothane. We believe, for cost considerations, that most anaesthetists initially reserved the use of isoflurane for specific clinical indications, such as ischaemic heart disease, Caesarean section, or neurosurgery. We reasoned that the increased publicity that concerned halothane hepatitis and the continuing debate[2–4] with the CSM would significantly alter anaesthetists' choice or use of volatile agents and lead to a swing towards the more expensive enflurane, and particularly isoflurane whose advertising stressed its safety when administered repeatedly. The cost of isoflurane inflated by a factor of approximately two during this period, at the same time as one supplier (Anaquest) stopped marketing it in the UK. The price of enflurane increased even more (Table 1).

We investigated whether the use of volatile agents had changed over this 3-year period and what was the anaesthetists' perceived usage of these agents. We obtained pharmacy and management data that related to their use and to the total number of general anaesthetics delivered in this Health Authority. We conducted surveys of practice, of consultants in our own Health Authority, and of a group of senior registrars, who might be more influenced by publicity, but who had sufficient length of service in anaesthesia to have witnessed a change in practice.

### *Method*

Pharmacy data for the years 1985–86, 1986–87, and 1987–88 was available to show the consumption and cost of the three agents. The pharmacies in the Health Authority have operated a tight 'topping-up' system for the last 5 years. We calculated the number of MAC hours of anaesthesia available in each year for each agent from the volume of liquid anaesthetic agents distributed. We assumed a fresh gas flow of 7 litres/minute for this calculation (see Addendum). This flow was chosen from a knowledge of common practice in this Health Authority. The number of general anaesthetics delivered was available directly from Health Authority records for the years 1986–87 and 1987–88, but the figures for 1985–86 were obtained from operating theatre summaries in all 11 sites where anaesthetics are administered in this Health Authority. Equivalent time spans (April–April) were used. These figures allowed calculation of the 'quantity' of anaesthesia (as MAC hour anaesthetic) delivered for each anaesthetic.

Independently, we surveyed our own consultant anaesthetists and all 19 senior registrars in anaesthesia employed by the Northern Regional Health Authority. Our own consultants were questioned directly, while the senior registrars were surveyed by telephone. We asked questions that concerned their perceived use of volatile agents, and,

**Table 1.** Unit cost (£100 ml) for volatile agents 1985–86 to 1987–88.

| | Halothane | Enflurane | Isoflurane |
|---|---|---|---|
| 1985–86 | £2.70 | £7.50 | £23.00 |
| 1986–87 | £2.60 | £15.30 | £38.50 |
| 1987–88 | £2.50 | £15.30 | £38.50 |

Correspondence should be addressed to Dr P.G. Lawler please.
Accepted 20 January 1989.

**Table 2.** Questionnaire.

We are surveying volatile anaesthesia use in the last 3 years.
Name: Grade:
Year qualified (SR): Years in anaesthesia:
(1) Has your use of the volatile agents halothane, enflurane or isoflurane changed in the last 3 years?
Yes/No.................If No go to 4
If 'Yes'
(2) (a) Has your use of halothane:
increased*/decreased*/remained the same?
(b) Has your use of enflurane:
increased*/decreased*/remained the same?
(c) Has your use of isoflurane:
increased*/decreased*/remained the same?
*score: 0 for no change,
− for small decrease, − − for large decrease
+ for small increase, + + for large increase
(3) Is this change *mainly* due to:
(a) change in overall (total) use of volatile agents
(b) medicolegal reasons
(c) clinical reasons
(d) another reason
(4) Do you ever use any other agents: Y/N
if Y: what?

should the respondent have indicated a change, why this had occurred. The questionnaire, which was rigidly applied, is shown (Table 2). Answers were graded. The detailed reasons behind the survey were not given until completion of the questionnaire and only if a request was made.

### *Results*

The total number of general anaesthetics delivered in the surveyed period increased from 21 302/annum in 1985–86 to 24 901/annum in 1987–88, an increase of 11%. Expressed as liquid anaesthetic, halothane consumption remained constant in the first 2 years, but decreased in the third. On the other hand, enflurane consumption increased in the first year, but did not increase thereafter. There was a progressive increase in isoflurane usage (Table 3). Halothane accounted for 77.4% of anaesthetics in the first year, 69.6% in the second and 56.7% in the third, when these data are expressed as quantity of anaesthesia delivered (MAC hours). For enflurane, the corresponding figures were 18.8% in the first year, and 23.5% and 28.3% in the second and third years respectively. The equivalent annual figures for isoflurane were 2.9%, 6.9% and 15% (Fig. 1, Table 4). The quantity, when total MAC hours of volatile agent delivered for each anaesthetic was calculated, was 1.078 MAC hour anaesthetic in the first year, 1.119 MAC hour anaesthetic in the second, but only 0.89 MAC hour anaesthetic in the last year (Table 4).

The survey of our consultants showed that all had changed their practice. All but one considered that they had used very much less halothane; the one who had not changed his use of halothane seldom used it previously. Consultants were evenly divided as to why they had changed; half had done so for medicolegal reasons and half for clinical reasons. Consultants believed they had increased their use of enflurane, but considered that isoflurane usage had increased, relatively much more. No one believed they had made any overall change in the use of vapours (Table 5).

**Table 3.** Total usage (ml) of volatile agents 1985–86 to 1987–88.

| | Halothane | Enflurane | Isoflurane |
|---|---|---|---|
| 1985–86 | 263 250 | 171 750 | 18 300 |
| 1986–87 | 265 000 | 230 250 | 47 000 |
| 1987–88 | 186 000 | 239 250 | 88 400 |

**Table 4.** Quantity of anaesthesia delivered, 1985–86 to 1987–88.

| | 1985–86 | 1986–87 | 1987–88 |
|---|---|---|---|
| Total GAs | 21 302 | 22 961 | 24 901 |
| Halothane<br>MAC hours (%) | 17 770.35<br>(77.41%) | 17 888.48<br>(69.63%) | 12 555.69<br>(56.67%) |
| Enflurane<br>MAC hours (%) | 4495.25<br>(18.76%) | 6026.38<br>(23.46%) | 6261.94<br>(28.27%) |
| Isoflurane<br>MAC hours (%) | 690.49<br>(2.88%) | 1773.38<br>(6.90%) | 3335.47<br>(15.05%) |
| Total MAC hours | 22 956.09 | 25 688.24 | 22 153.1 |
| MAC hours/GA | 1.078 | 1.1187 | 0.8896 |

Senior registrars' views were more varied. Four stated that they had made no changes in practice. The 15 who believed that they had changed, had reduced their use of halothane usually in favour of isoflurane. There appeared to be some discrepancy between the reduction given for halothane and the increases stated for the other vapours. Only one respondent considered he had reduced his overall use of volatile agents. They were equally divided in their reasons for change i.e. clinical or medicolegal. The majority of anaesthetists in both groups used no other volatile agent; if they did, the agent used was usually trichloroethylene (Table 6).

The costs of our volatile agents increased considerably during this period, from £24 776 in 1985–86 to £64 417 in 1987–88 (Fig. 2, Table 7). Isoflurane accounted for 53% of this cost in 1987–88, compared with only 19% in 1985–86. On the other hand, even in 1985–86, halothane only accounted for 29% of the total cost. This decreased to 7.2% in 1987–88.

### *Discussion*

This study provides an insight into the use of volatile agents in this District. There was negligible use of other agents such as trichloroethylene and anaesthetic di-ethyl ether between 1985 and 1988. Thirty-two bottles of the

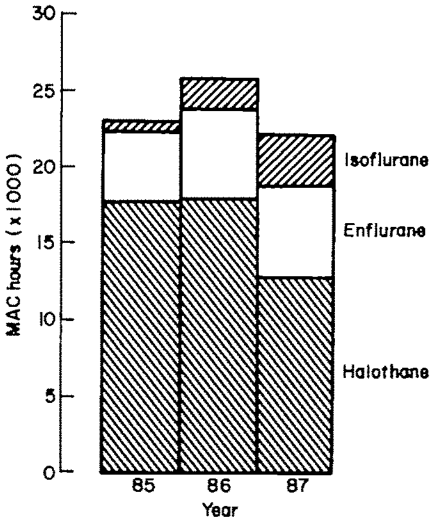


**Fig. 1.** Quantity of anaesthesia, expressed as MAC hours, for each agent, delivered in each of the 3 years.

**Table 5.** Results of questionnaire: consultants.

| | Consultant | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| *Questions* | | | | | | | | | | | | | | | |
| (1) Change | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y |
| (2a) Halothane | – – | – – | – – | – – | 0 | – – | – | – – | – | – – | – | – – | – – | – | – |
| (2b) Enflurane | + + | + + | + + | + + | + | + | – | + | – | + | 0 | + + | 0 | + | + |
| (2c) Isoflurane | + + | + + | + | + + | + + | + + | + | + + | + + | + + | + | + | + + | + + | 0 |
| (3a) Reduction | N | N | N | N | N | N | N | N | N | N | N | Y | N | N | N |
| (3b) Clinical | Y | Y | N | Y | N | N | N | N | N | Y | Y | N | N | Y | N |
| (3c) Medicolegal | N | N | Y | Y | N | Y | Y | Y | Y | N | N | N | Y | N | Y |
| (3d) Other | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| (4) Other agents | N | Y | Y | N | N | N | N | N | N | N | Y | Y | Y | N | N |

Y, yes; N, no; (–) small decrease; (– –) large dcecrease; (+) small increase; (+ +) large increase.

**Table 6.** Results of questionnaire: senior registrars.

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Questions* | | | | | | | | | | | | | | | | | | | |
| (1) Change | Y | N | Y | N | Y | Y | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | N | Y |
| (2a) Halothane | – – | 0 | – – | 0 | – – | – – | – – | – – | – – | – – | – – | 0 | – – | – – | 0 | – – | – – | 0 | – – |
| (2b) Enflurane | + | 0 | + + | 0 | 0 | + | + | + | + + | 0 | + + | 0 | 0 | 0 | – | + | 0 | 0 | + + |
| (2c) Isoflurane | + | 0 | + + | 0 | + + | + + | + | + + | + + | + + | + | 0 | + + | + + | + + | + + | + + | 0 | + |
| (3a) Reduction | N | N | N | N | N | N | N | N | N | N | N | N | N | N | Y | N | N | N | N |
| (3b) Clinical | Y | N | N | N | Y | N | N | Y | Y | N | N | N | Y | N | N | Y | N | N | Y |
| (3c) Medicolegal | N | N | Y | N | N | Y | Y | N | N | Y | Y | N | N | Y | N | N | Y | N | N |
| (3d) Other | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| (4) Other agents | N | N | Y | N | N | N | N | Y | N | N | N | Y | N | Y | N | Y | N | Y | N |

Y, yes; N, no; (–) small decrease; (– –) large decrease; (+) small increase; (+ +) large increase.

former and only one of the latter were bought. No cyclopropane was purchased.

Our study is open to various interpretations. The CSM's recommendations on halothane came in the centre of the 1986–87 year (September 1986). The abrupt decrease in halothane usage between 1986–87 and 1987–88, or the coincident increase in isoflurane use shown by our survey, may have been gradual and uninfluenced by the CSM.

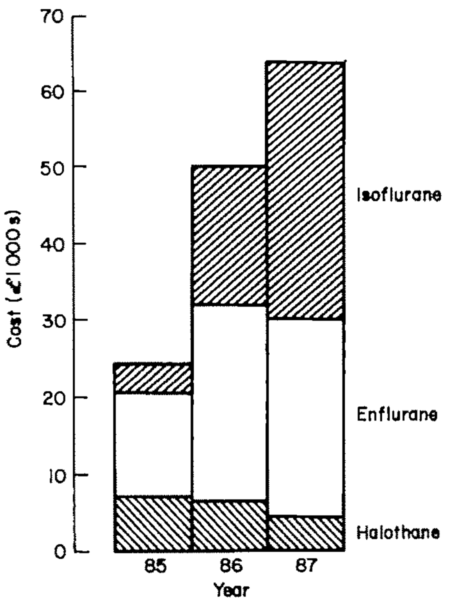


**Fig. 2.** Costs of each agent in each of the three periods reviewed.

Unfortunately, we were unable to obtain monthly pharmacy data for the year 1986–87 when changes might have been expected to occur, so we cannot say whether the change registered was abrupt or gradual.

Our survey confirms a change in the actual use of our primary volatile anaesthetic agents, halothane, enflurane and isoflurane. The higher MAC values of enflurane and isoflurane have obvious effects upon consumption since more liquid anaesthetic is necessary to produce 'anaesthesia'. We assumed a fresh gas flow of 7 litres/minute in the calculation of MAC hours. Higher than minimum flows would have been used since capnography was not generally available in this period. The Bain system is usually used only in the anaesthetic room in this Health Authority.

There seem only marginal differences between the perceived changes made by our own consultants and by the senior trainees interviewed. However, the changes in practice shown by the pharmacy data appear considerably less than would have been predicted from our survey.

**Table 7.** Annual expenditure on halothane, enflurane and isoflurane, for the years 1985–86 to 1987–88. (£.p. and % of total expenditure).

| | Halothane (%) | Enflurane (%) | Isoflurane (%) | Total |
|---|---|---|---|---|
| 1985–86 | £7128.81<br>(28.77%) | £13 038.26<br>(52.62%) | £4609.00<br>(18.6%) | £24 777.07 |
| 1986–87 | £6890.00<br>(13.72%) | £25 320.35<br>(50.42%) | £18 104.40<br>(36.05%) | £50 214.75 |
| 1987–88 | £4664.58<br>(7.24%) | £25 701.95<br>(39.90%) | £34 051.24<br>(52.86%) | £64 417.77 |

Halothane still appears to account for well over 50% of the anaesthesia.

Anaesthetic delivery was highest in 1986–87, and decreased in 1987–88. This suggests a reduction in the number of volatile anaesthetics delivered, although the local perception was of no change in the proportion of volatile anaesthetics given, or of our gas flows. Recalculation of anaesthetic delivery as MAC hours anaesthetic showed that in 1987–88 we did not appear to be giving 'sufficient' anaesthesia (i.e. one 'MAC'). MAC hour anaesthetic was below one (0.89) in 1987–88, which compared with 1.08 and 1.12 MAC hours anaesthetic in 1985–86 and 1986–87. Unfortunately, we have no way of knowing the total hours of anaesthesia delivered, so we have no way to quantify the average level of anaesthesia during an anaesthetic (MAC hours hour). Furthermore, this method of expression of our quantity of anaesthesia takes no account of the adjuvant effect of nitrous oxide, although (outside obstetric anaesthesia) few anaesthetists use less than 60% or more than 70% nitrous oxide. However, this 'error' is common to all years.

The changes in MAC hours anaesthetic might mean many shorter anaesthetics, but this was not our perception. However, this observation might suggest a swing away from volatile agents during routine anaesthetics, perhaps because of expense. The expected consequence would be a tendency to use intravenous anaesthesia alone, or volatile anaesthesia supplemented by additional opioid. There was a marked increase in theatre use of the opioid supplement alfentanil over the last two periods, but none in fentanyl. Further enquiries in the pharmacy revealed a great increase in the use of propofol, which suggests that many anaesthetics of short duration might be unsupplemented with a significant quantity of volatile agent. Total intravenous anaesthesia over significant durations (i.e. beyond a few 'top-ups') was not practised in this period.

The price of isoflurane has had a significant affect upon our pharmacy costs. Halothane accounted for 28.77% of total expenditure on volatile anaesthetic agents in 1985–86, but by 1987–88 it accounted for only 7.24% of the total cost. This large percentage change disguises the relatively small decrease in expenditure on halothane; this fell by only 35%, from £7128 in 1985–86 to £4664 in 1987–88. Our total volatile agent expenditure increased in the same period from £24 776 in 1985–86 to £64 417 in 1987–88, an increase of 260%. Our enflurane expenditure only increased between 1985–86 and 1986–87 (from £13 038 to £25 320) and was unchanged in 1987–88 (£25 701), so most of this change was accounted for by isoflurane. The average cost of volatile agent/anaesthetic more than doubled over the period, and increased from £1.16 in 1985–86 to £2.59 in 1987–88. MAC for MAC, isoflurane is currently over 23 times more expensive than halothane. Enflurane is nearly 14 times more expensive.

## References

1. Committee on Safety of Medicines. Halothane hepatotoxicity. *Current Problems 18* 1986; Sept: 1–2.
2. Adams AP, Campbell D, Clarke RSJ, Downing JW, Healy TEJ, Hull CJ, Hutton P, Jones JG, Norman J, Payne JP, Robson G, Spence AA, Vickers MD. Halothane and the liver. *British Medical Journal* 1986; **293:** 1023.
3. Rosen M. Guidelines on halothane. *British Medical Journal* 1987; **294:** 836.
4. Spence AA. Halothane. *British Journal of Anaesthesia* 1988; **61:** 124.

### *Addendum*

*Calculation of agent consumption, expressed as MAC hours.* In one hour, the volume of anaesthetic vapour (ml) delivered from a vaporizer set at 1 MAC (% v.v) is equal to:

$$(F \times 1000) \times (MAC/100) \times 60 \text{ ml}$$

where F is the input carrier flow in litres/minute.

Each mol of liquid anaesthetic agent yields 22.4 litres of vapour at STP, or 24 litres at a theatre temperature of 20°C (22.4 × 293/273).

Each mol of liquid agent has a volume of (MW/SG) ml where:

MW is the molecular weight and
SG is the specific gravity of the liquid agent

Each litre of vapour is thus produced from [(MW/SG)/24] ml liquid agent.

Therefore:

One hour's anaesthesia at one MAC, at a fresh gas flow of F litres/minute requires:

$$\{[(MW/SG) \times (MAC/100) \times (F \times 1000) \times 60]/24\} \text{ ml liquid agent.}$$

For the agents used, and assuming a carrier gas flow of 7 litres/minute, the volumes of liquid anaesthetic required to supply anaesthesia at one MAC for one hour (one MAC hour) are:

halothane: 14.81 ml
enflurane: 38.21 ml
isoflurane: 26.50 ml

---

*Anaesthesia,* 1989, Volume 44, pages 599–602

# Cardiovascular response during cerebral angiography under general and local anaesthesia

D. G. Clayton, FFARCS, B. M. O'Donoghue, FFARCS, J. E. Stevens, FFARCS, Senior Registrars, Department of Anaesthesia, P. E. Savage, FRCS, Senior Registrar, Department of Radiology, Atkinson Morley's Hospital, London SW20.

## Summary

*Nineteen patients with subarachnoid haemorrhage who had cerebral angiography with the new contrast medium iohexol, were randomly allocated to receive either local anaesthesia plus sedation, or general anaesthesia. Arterial blood pressure,* $Pa\text{O}_2$, $Pa\text{CO}_2$

*and patient acceptability were examined. Significant fluctuations in arterial blood pressure occurred in the patients who received general anaesthesia. Local anaesthesia was associated with a stable blood pressure, adequate spontaneous ventilation and good patient acceptability. The quality of films obtained was examined and found to be of good or very good diagnostic quality in all cases in both groups of patients. Greater use of local anaesthesia with sedation for angiography is recommended.*

**Key words**

*Anaesthesia;* neuroradiology.
*Brain;* blood flow, intracranial pressure.

The aims of anaesthetic techniques for neuroradiology include the avoidance of fluctuations in arterial blood pressure, the prevention of hypoxia, hypercapnia and increased venous pressure. It is desirable, in addition, for the technique to permit a neurological assessment to be made during and immediately after the procedure. The greatest complication of this procedure is rebleeding from a cerebral aneurysm leading to permanent neurological sequelae or death. The incidence of rebleeding in one study was 2.4 times as great when general anaesthesia was used compared to when local anaesthesia was used.[1] The patient, from the radiologist's standpoint, should be able to cooperate by holding his breath and refraining from swallowing during contrast injections. It is also stated that controlled hyperventilation during general anaesthesia improves the quality of angiograms in comparison with similar procedures performed without hyperventilation.[2]

Early ionic contrast media such as meglumine iothalmate and metrizamide proved to be unpleasant and cause pain and a burning sensation on injection into the common carotid artery. The incidence of these unpleasant effects has been greatly reduced with the introduction of nonionic preparations such as iohexol.[3-5] It is also reported that meglumine iothalmate and the earlier ionic compound, metrizamide, may cause more cardiovascular instability than iohexol.[3,4] Thus, the new nonionic contrast media are ideally suited to local anaesthesia for cerebral angiography.

This study was designed to compare the cardiovascular responses to general anaesthesia or local anaesthesia plus sedation, in patients with subarachnoid haemorrhage who had cerebral angiography, and was approved by the local ethics committee. The adequacy of films for clinical requirements was also examined in the two groups.

## *Methods*

Nineteen patients aged 18–65 years were randomly allocated to general anaesthesia or local anaesthesia plus sedation. They entered into the study according to the following criteria: the diagnosis of subarachnoid haemorrhage was confirmed by lumbar puncture (LP) and computerised tomography (CT); all patients were grade 1 or 2 cases according to the scale of Hunt and Hess[6] i.e. minimal to severe, generalised or nuchal headache with no neurological deficit; there was no history of cardiorespiratory disease, metabolic disorder or long-term medication.

Both groups received pre-operative medications of glycopyrronium 0.2 mg one hour before examination. Age, weight and resting arterial blood pressure were noted in the angiography suite. A 20-gauge cannula was placed in the radial artery, after local infiltration with 1% lignocaine, and connected via a Gaeltec pressure transducer to a Roche 128 Pressure and ECG monitor. Continuous recording of blood pressure was obtained on a Toa EPR-152A dual channel chart recorder, and baseline values were established over a 5-minute interval.

General anaesthesia was induced with fentanyl 1.5 μg/kg, droperidol 0.1 mg/kg and thiopentone 4–5 mg/kg. Muscle relaxation was effected with vecuronium 0.1 mg/kg. The larynx and trachea were sprayed with 10% lignocaine prior to intubation. Anaesthesia was maintained with 65% nitrous oxide in oxygen, delivered by intermittent positive pressure ventilation from a Manley Pulmovent ventilator. Supplements of fentanyl (25 μg) and vecuronium (2 mg) were administered as clinically indicated. End-tidal $CO_2$ was monitored continuously by a Gould capnograph, and minute ventilation adjusted to maintain the $F_{E'}CO_2$ at 0.04–0.045 $P_{aO_2}$ and $P_{aCO_2}$ were measured every 30 minutes by blood gas analysis. Neuromuscular blockade was reversed at the end of the procedure with 2.5 mg neostigmine and 1.2 mg atropine. Monitoring was continued for one hour after the procedure.

Diazepam emulsion 0.1 mg/kg was given intravenously in the local anaesthetic group and oxygen was added to the inspired air by an MC mask on arrival in the angiography suite before placement of the radial artery cannula, as detailed above. The femoral cannulation site was infiltrated with 2% lignocaine 5 ml, and supplements of diazepam emulsion were repeated up to a maximum of 10 mg. Observations were as for the general anaesthetic group with the exception of $F_{E'}CO_2$. The patients were kept informed of proceedings and were able to cooperate with the radiologist throughout the procedure.

The arterial blood pressure recordings and the blood gas determinations in each group were analysed by the two-tailed Student's *t*-test.

All the available films were examined by an independent radiologist after completion of the study on cardiovascular responses. They were graded for diagnostic quality on a scale from poor to very good. Subtraction films were also examined where these were made. These results were analysed using the Chi-squared test.

## *Results*

Ten patients received general anaesthesia and nine local. Details of age, weight and resting mean arterial pressure are shown in Table 1.

Five phases of the procedure were noted in the general anaesthetic group, where changes of arterial pressure occurred. These were related to induction, tracheal intubation, angiography, reversal and recovery (Table 2). Significant changes in mean arterial pressure (MAP) occurred on

**Table 1.** Details of patients, mean (SEM).

| | General anaesthesia | Local anaesthesia |
|---|---|---|
| Number of patients | 10 | 9 |
| Age, years | 50.2 (4.4) | 45.6 (3.9) |
| Weight, kg | 66 (2.2) | 65.8 (3.3) |
| MAP, mmHg | 88.7 | 96.8 |

MAP, mean arterial pressure.

Accepted 6 December 1988.

**Table 2.** Change in mean (SEM) arterial pressure (MAP) during the five phases in the general anaesthesia group, which caused significant ($p<0.05$) changes marked*.

| | Induction | Intubation | Angiography | Reversal | Recovery |
|---|---|---|---|---|---|
| MAP mmHg before event | 116.8 (3.5) | 89.5 (6.1) | 117.8 (5.2) | 89.1 (4.5) | 103 (7.5) |
| MAP change during event | −28.6 (4.7) | +37.5 (5.5) | +22.5 (3.1) | +20.2 (5.5) | −3.9 (7.2) |
| *t* | 6.066* | 5.492* | 7.363* | 8.702* | 0.546 |

induction, intubation, during angiography and on reversal. It is of note that the mean arterial pressure of patients in this group had increased from 88.7 mmHg to 116.8 mmHg prior to induction; this reflected the anxiety of patients about to undergo general anaesthesia.

Four phases of MAP were studied in the local anaesthetic group; these corresponded to the injection of local anaesthetic, to groin puncture, to removal of the femoral artery catheter with compression for 10 minutes, and to recovery. None of the pressure changes in this group were significant (Table 3). No significant blood pressure change could be related to injections of iohexol in either group.

The results of $Paco_2$ measurements are shown in Table 4. This was maintained at baseline levels in the general anaesthetic group by ventilation adjustment and no significant change occurred in the local group. Hyperventilation persisted in the latter patients during the procedure.

No study or angiography run had to be repeated because of patient movement. All films were well positioned and of diagnostic quality. Digital subtraction angiography (DSA) was only just being introduced at the time of this study, and thus no patient had DSA alone. All DSA films were good, but results were not analysed because of the small numbers. Subtraction angiograms, for which a still patient is absolutely necessary, were obtained in patients from both groups, and all were of good quality. The quality of angiogram films in the general and local anaesthetic groups are shown in Table 5. The differences between the groups did not reach statistical significance. Magnification films were not routinely obtained at the time of this study, thus no data on magnification films are presented.

### *Discussion*

This study demonstrates the very significant advantage of local anaesthesia over general anaesthesia for cerebral angiography in the maintenance of a stable arterial blood pressure. In particular, hypotension after induction and the pressor response to intubation were avoided.

Hypotension or hypertension can be extremely hazardous in subarachnoid haemorrhage which may be accompanied by impairment of cerebral autoregulation. Loss of autoregulation is most marked in grade 3 and grade 4 patients, but it can be observed in grade 1 and 2 patients, particularly where vasospasm is a feature.[7,8] Blood flow then becomes pressure dependent and hypotension may lead to a critical loss of blood flow, or paradoxically a localised increased flow due to the added effects of vasospasm. Voldby *et al.*[8] also noted that the response to $Paco_2$ was better maintained than the autoregulatory response, but found that hyperventilation did not reliably induce an inverse steal. The brain cells may be able to compensate to a certain extent for a decrease in blood flow by increasing oxygen extraction, but eventually ischaemia, lactic acidosis and cellular damage follow.

The effects of hypertension in subarachnoid haemorrhage have been less extensively studied. Arterial blood pressures above the autoregulatory range, which may be impaired, lead to higher pressures in the cerebral vessels. This in turn not only increases the risk of rebleeding from the aneurysm but also causes damage to the microvasculature in the blood brain barrier leading to the formation and extension of vasogenic oedema.[9,10]

The effects of these two anaesthetic techniques on intracranial pressure were not measured directly in this study, but it is well established that hypertension, coughing, straining, hypercarbia and volatile anaesthetic agents may increase intracranial pressure. Unstable blood pressure was a particular feature in the general anaesthetic group and although no pressures outside the normal autoregulatory range were recorded, it remains possible that swings in arterial pressure did produce significant increases in intracranial pressure due to compromised autoregulation. Coughing and straining occurred occasionally at tracheal extubation despite the use of topical lignocaine at induction and might also influence intracranial pressure by venous congestion. The results of blood gas estimations confirmed that hypercarbia was not a risk factor in either group.

It may be argued that the use of barbiturates and opiates in the general anaesthetic group could confer a measure of protection against cellular anoxia. Thiopentone decreases cerebral blood flow (CBF) and cerebral metabolic oxygen consumption rate ($CMRO_2$). However, at surgical levels of anaesthesia in humans, this reduction of $CMRO_2$ is of the order of 36–45% and is accompanied by a parallel reduction in CBF if $Paco_2$ is maintained constant.[11] Fentanyl may also reduce CBF and $CMRO_2$ but the effect is minimal at the dose level used in this study.[12] The effect of droperidol is less well defined but at doses of 0.3 mg/kg appears to reduce CBF with little effect on $CMRO_2$.[13] Conversely, general anaesthesia may have unfavourable effects by impairment of autoregulation, but this effect is probably minimal with the technique of light anaesthesia used in this study.

The possible effects of diazepam 0.1 mg/kg in the local anaesthetic group also requires examination. Diazepam was given to reduce the unpleasant effects of femoral cannulation, and any discomfort during the injection of

**Table 3.** Change in mean (SEM) arterial pressure (MAP) during the four phases in the local anaesthesia group, which caused swings in blood pressure. None of the changes are significant.

| | Injection of local anaesthesia | Puncture | Compression | Recovery |
|---|---|---|---|---|
| MAP mmHg before event | 98 (4.0) | 95.1 (4.1) | 99.5 (5.2) | 94.5 (5.0) |
| MAP change during event | −4.5 (2.2) | +3.0 (2.3) | −5.6 (4.0) | +8.3 (3.7) |
| *t* | 2.082 | 1.305 | 1.421 | 2.23 |

**Table 4.** Pre- and peroperative $P\text{aco}_2$ (mmHg) in the two groups, mean (SEM) and range, None of the changes are significant

| | Pre-operative | 30 minutes | 60 minutes |
|---|---|---|---|
| General anaesthesia | 32 (1.2) | 31.7 (1.5) | 33.4 |
| $P\text{aco}_2$ | 24–39 | 23–39 | 31–37 |
| Local anaesthesia | 32 (1.6) | 34 (0.95) | 35.3 (1.8) |
| $P\text{aco}_2$ | 24–38 | 30–37 | 30–41 |

contrast medium. It is known that the intravenous administration of 50 mg may decrease CMRO$_2$ by 25% in comatose patients with diffuse brain damage.[14] Reduction in CMRO$_2$, at a dose of 10 mg, is accompanied by a parallel decrease in CBF. It seems unlikely that the lower dosage in this study produced any significant effect. The results of blood gas analysis indicate that diazepam did not produce depression of ventilation. The use of diazepam before insertion of the local anaesthetic may well have contributed to the remarkable stability of this group. Diazepam might well have reduced the hypertensive increase on induction if it had been used before induction in the general anaesthetic group. However, it would be less likely to have altered the later instability.

A further significant advantage of the local anaesthetic technique was the ability to monitor neurological status throughout the procedure. Neurological deterioration, which may occur with vasospasm, increasing cerebral oedema or rebleeding, should be readily detectable and if necessary the procedure can be abandoned. Rupture of an aneurysm during angiography is not a common complication, but in a survey of world literature in 1976 Wilkins refers to 41 cases.[15] Deterioration may only be detectable with general anaesthesia when it is sufficient to cause cardiovascular sequelae. No procedure had to be abandoned in this study and no adverse reactions to iohexol occurred.

The use of iohexol in neuroradiology has been studied by several authors.[3–5] The older ionic media were associated with appreciable pain and burning sensations on injection, which hitherto caused us to prefer general anaesthesia for cerebral arteriography in this unit. The patients in this study were warned that they might experience discomfort on injection of iohexol under local anaesthesia but none found this unacceptable. The cardiovascular stability of patients given iohexol was confirmed, which enhanced the greater stability observed in patients given local rather than general anaesthesia.

The rationale for preferring general anaesthesia with hyperventilation to slow the circulation and thus improve the diagnostic quality of the films has been put forward by Edmonds-Seal *et al.*[2] Our results show that for both ordinary angiography and subtraction angiography, films of good diagnostic quality were obtained in all cases in both groups, with no significant difference between them. A major difference between the two groups in this study, and those reported by Edmonds-Seals *et al.*[2] was the $P\text{aco}_2$ in the nonventilated patients. The patients in this study who received local anaesthesia spontaneously hyperventilated to a $P\text{aco}_2$ of 32–35 mmHg, whereas the spontaneously breathing patients in Edmonds-Seals' group were anaesthetised, and had a mean $P\text{aco}_2$ of 50.5 mmHg. The results in Table 5 do show a tendency for better quality films to be obtained in anaesthetised, ventilated patients, and it may be argued that with larger groups the difference would be significant. It is, however, our contention that if films of good and very good diagnostic quality are reliably obtained using local anaesthesia, the marginal benefits of general anaesthesia are outweighed by its disadvantages.

**Table 5.** Number of carotid or vertebral angiogram films compared for quality in the general and local anaesthetic groups. (NB. Not all patients had films available for assessment and some patients had both carotid and vertebral angiograms assessed).

| Group | Good | Very good |
|---|---|---|
| Local anaesthesia | 8 | 2 |
| General anaesthesia | 4 | 4 |

Chi-squared, 1.8; p > 0.1.

We believe that general anaesthesia should only rarely be necessary for cerebral angiography and that with the introduction of nonionic contrast media, the majority of patients will benefit from the use of a local anaesthetic technique.

## *Acknowledgments*

We thank Drs J. Ambrose, G. R. Hart and J. Britten, Consultant Neuroradiologists, for their advice and helpful comments and Miss L. Stevens for statistical guidance.

## *References*

1. Perret G, Nishioka H. Report on the cooperative study of intracranial aneurysms and subarachnoid hemorrhage. Section IV Cerebral angiography. *Journal of Neurosurgery* 1966; **25:** 98–114.
2. Edmonds-Seal J, du Boulay G, Bostick T. The effect of intermittent positive pressure ventilation upon cerebral angiography with special reference to the quality of the films—a preliminary communication. *British Journal of Radiology* 1967; **40:** 957–8.
3. Bryan RN, Miller SL, Roehm JO Jr., Weatherall PT. Neuroangiography with iohexol. *American Journal of Neuroradiology* 1983; **4:** 344–6.
4. Hindmarsh T, Bergstrand G, Ericson K, Olivecrona H. Comparative double-blind investigation of meglumine metrizoate, metrizamide, and iohexol in carotid angiography. *American Journal of Neuroradiology* 1983; **4:** 347–9.
5. Pelz D, Fox AJ, Viñuela F. Clinical trial of Iohexol vs. Conray 60 for cerebral angiography. *American Journal of Neuroradiology* 1984; **5:** 565–8.
6. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *Journal of Neurosurgery* 1968; **28:** 14–20.
7. Nornes H, Knutzen HB, Wikeby P. Cerebral arterial blood flow and aneurysm surgery. Part 2. Induced hypotension and autoregulatory capacity. *Journal of Neurosurgery* 1977; **47:** 819–27.
8. Voldby B, Enevoldsen EM, Jensen FT. Cerebrovascular reactivity in patients with ruptured intracranial aneurysms. *Journal of Neurosurgery* 1985; **62:** 59–67.
9. McDowall GD. Neurosurgical anaesthesia and intensive care. In: Hewer CL, Atkinson RS, eds. *Recent advances in anaesthesia and analgesia,* Number 12. Edinburgh: Churchill Livingstone, 1970: 16–43.
10. Schutta HS, Kassell NF, Langfitt TW. Brain swelling produced by injury and aggravated by arterial hypertension. A light and electron microscopic study. *Brain* 1968; **91:** 281–94.
11. Messick JM, Newberg, LA, Nugent M, Faust RJ. Principles of neuroanaesthesia for the nonneurosurgical patient with CNS pathophysiology. *Anaesthesia and Analgesia* 1985; **64:** 143–74.
12. Freeman J, Ingvar DH. Effects of fentanyl on cerebral cortical blood flow and EEG in the cat. *Acta Anaesthesiologica Scandinavica* 1967; **11:** 381–91.
13. Michenfelder JD, Theye RA. Effects of fentanyl, droperidol and Innovar on canine cerebral metabolism and blood flow. *British Journal of Anaesthesia* 1971; **43:** 630–6.
14. Maekawa T, Sakabe T, Takeshita H. Diazepam blocks cerebral metabolic and circulatory responses to local anesthetic-induced seizures. *Anesthesiology* 1974; **41:** 389–91.
15. Wilkins RH. Aneurysm rupture during angiography: does acute vasospasm occur? *Surgical Neurology* 1976; **5:** 299–303.

*Anaesthesia*, 1989, Volume 44, pages 603–605

# Reversal of prolonged sedation using flumazenil in critically ill patients

A. Bodenham,* MB, BS, FFARCS, Research Registrar, G. R. Park, FFARCS, Consultant, Department of Anaesthesia, Addenbrooke's Hospital, Cambridge CB2 2QQ.

## Summary

*Thirteen critically ill patients received flumazenil after multiple doses, or an infusion, of midazolam was used as part of a sedation regimen to facilitate intensive care. All patients remained excessively sedated after the midazolam was stopped for 6 hours or longer. An improvement in conscious level occurred in eight patients (61%). In four of these eight patients, the duration of action of flumazenil necessitated its continued administration by an infusion to maintain the improvement in conscious level. The dose of flumazenil required each hour was less than estimated previously; this indicates that it may be subjected to similar alterations of elimination as those described for midazolam. Flumazenil appears to be a useful drug for the reversal of prolonged benzodiazepine sedation but repeated bolus doses or an infusion are needed if significant accumulation of benzodiazepines has occurred.*

**Key words**
*Intensive care.*
*Hypnotics*; midazolam.

Midazolam, a benzodiazepine with a short duration of action, is used frequently to provide sedation in critically ill patients. The principal metabolite is α-hydroxymidazolam, which is believed also to be active in man.[1] Prolonged sedation after midazolam administration is a recognised problem in the critically ill despite the short duration of action of the drug in healthy patients.[2,3] In addition, 6–10% of the population have a pharmacogenetic abnormality which results in slow metabolism of midazolam.[4] Both these factors may result in accumulation when a continuous intravenous infusion is administered, and may result in excessive sedation, difficulty in assessment of neurological function, problems with weaning from artificial ventilation and cardiovascular instability. Furthermore, unnecessarily long periods of sedation increase the duration of admission to the intensive care unit, with inefficient utilisation of that resource.

Benzodiazepine sedation is reversible with the benzodiazepine antagonist flumazenil which has been available commercially for some time in Europe.

We administered flumazenil to 13 critically ill patients who remained undesirably sedated after administration of multiple doses or an infusion of midazolam. The midazolam had been stopped for a variable time period of 6 to 72 hours.

### *Method*

Patients were included in this prospective study when they were known to have received during their treatment period significant doses of midazolam which might have contributed to excessively prolonged sedation. Flumazenil was given after a reasonable time for recovery had passed or when it was desirable to awaken the patient for other reasons (neurological assessment, to enhance coughing ability, or to improve ventilatory effort to aid weaning from artificial ventilation).

Patients with known hypertension or ischaemic heart disease were excluded because of the theoretical risk of acute hypertension or myocardial ischaemia which may follow rapid awakening. If a tracheal tube was in place, an isoflurane vaporizer was connected to the ventilator system, to allow rapid resedation if cardiorespiratory instability developed on re-awakening. Analgesia was provided with intercostal nerve blocks if there was a recent abdominal surgical incision. Blood pressure was measured continuously in all patients by means of an intra-arterial cannula, and heart rate and cardiac rhythm were displayed on an electrocardiogram.

Opioids may cause prolonged sedation in critically ill patients, in particular those with renal failure.[5-7] Consequently, patients who were thought to have opioid-related sedation were given naloxone in 0.1-mg increments to a maximum of 0.4 mg for reversal of sedation. If there was no significant improvement with naloxone, flumazenil was given in 0.1-mg increments until satisfactory awakening occurred or a total of 1 mg was given.

The APACHE II score[8] without the Glasgow coma scale (GCS) component was recorded before the administration of naloxone and flumazenil. The GCS component of the APACHE II score may be an entirely reversible element if it is due to excessive sedation and so may increase the score inappropriately.[9]

Sedation was assessed before and after administration of naloxone and flumazenil using a score modified from that described by Ramsay *et al.*[10] (Table 1). An improvement in conscious level was defined as an increase of more than three points on the scale.

### *Results*

The 13 patients studied were of a heterogeneous nature (Table 2). Eight (61%) of the 13 showed an improvement of more than three points on the sedation scale after the

---

*Currently Senior Registrar in Intensive Care, Yorkshire Regional Health Authority.

Correspondence should be addressed to Dr G.R. Park.
Accepted 11 January 1989.

**Table 1.** Sedation score used to assess change in conscious level of critically ill patients after the administration of flumazenil. A significant response was defined as an increase of three points or more.

1. Alert, writing coherent messages
2. Alert, writing meaningless but legible letters
3. Alert, writing unintelligible scrawl
4. Alert, unable to write
5. Awake, but confused
6. Awake, agitated
7. Awakens with soft spoken voice
8. Awakens with loud voice
9. Awakens with gentle shaking
10. Awakens with glabellar tap
11. Responds to fingernail pressure in a purposeful way
12. Responds to fingernail pressure in an unpurposeful way
13. Does not respond to fingernail pressure

**Table 2.** Details of the 13 patients who received flumazenil to reverse the effects of midazolam. Data are presented as mean (SD).

| | |
|---|---|
| Females/males | 8/5 |
| Age, years | 49.2 (19.6) |
| APACHE II | 18.6 (5.8) |
| APACHE II without GCS | 10.6 (4.1) |
| Duration of sedation, days | 5.6 (5.2) |
| Time since last midazolam administration, hours | 28 (24) |
| *Presenting diagnosis* | |
| Liver transplant recipient | 5 |
| Multiple trauma | 3 |
| Colonic surgery | 3 |
| Septicaemic shock | 2 |

administration of flumazenil. The short duration of action of flumazenil led to resedation in seven of these patients within one hour of its administration. One patient required resedation with isoflurane when she bit her tracheal tube and caused partial airway obstruction. Four patients received an infusion of flumazenil to maintain the improvement in conscious level (Table 3). The infusions were required for a period of 8 hours to 10 days and were given at a rate of 0.5–1 mg/hour. The patient who required flumazenil for 10 days has been reported previously.[11] The success of flumazenil could not be related in a consistent pattern to age, sex, pathological processes, or APACHE II score due to the wide interpatient variability. In addition, the midazolam dosage, duration of sedation and time after discontinuation of midazolam did not correlate with the effects of flumazenil.

There were no unwanted effects of flumazenil such as nausea and vomiting in any of these patients. Blood pressure and heart rate increased in five patients by 5–20 mmHg and 12–25 beats/minute respectively.

Eleven patients received significant quantities of opioids during the sedation period. These patients received naloxone to evaluate whether opioid-related sedation was present. Two patients (18%) exhibited an improvement in conscious level of two points after naloxone but showed no further improvement with flumazenil.

Five patients did not respond to the administration of flumazenil. One of these had received a liver transplant. The donor organ had been ischaemic for an unusually prolonged period before revascularisation during the donor operation. He was sedated for 48 hours postoperatively. A cranial computerised tomogram was obtained when he did not awaken after flumazenil, and this showed possible cerebral oedema. Consequently, his lungs were ventilated artificially to produce hypocapnia ($Pa\text{CO}_2$ 3.5–4.5 kPa); neuromuscular blockade was used to prevent coughing and struggling, and opioids to provide sedation. He had awoken when the myoneural blocking agents were reversed 48 hours later. A second patient had also undergone liver retransplantation due to chronic rejection after her first transplant (for primary biliary cirrhosis). She required small doses of both morphine and midazolam after operation; only 10 mg of each was given in the first 24 hours. She did not respond to either flumazenil or naloxone but awoke spontaneously 12 hours later. One patient who underwent a difficult hemihepatectomy, complicated by a 30-litre blood loss, did not show any improvement in consciousness when either antagonist was administered, and did not make a spontaneous neurological recovery. It was thought that the coma was due to progressive hepatic failure and encephalopathy, and eventually the patient died without regaining consciousness. One patient had suffered massive trauma that necessitated bilateral lower limb amputations and several extensive operations to deal with the degloving injury to her abdomen. A minor head injury was sustained also. She developed acute renal failure as a consequence of these injuries. She had received large amounts of both midazolam and opioids; large, but carefully titrated, doses of flumazenil (5 mg) and naloxone (1.2 mg) had no effect. She regained consciousness spontaneously one week later. One patient required intensive care after a difficult colectomy for diverticular disease. There were extensive adhesions within the abdomen and the operation was complicated by excessive bleeding (15 litres). Her trachea was extubated after 48 hours of ventilatory support, but she became progressively confused with deterioration in her respiratory function. She received flumazenil at this time in an attempt to reverse any residual effects of benzodiazepines (including the confusion) and to try to avoid the need for reinstitution of ventilatory support. There was no response to the flumazenil, and ventilatory support was restarted. She awoke gradually over the next 48 hours.

## *Discussion*

Flumazenil is a specific benzodiazepine receptor antagonist. It has been shown to be a safe agent for the reversal of short-term benzodiazepine sedation in patients who require intensive care.[12] The only adverse effects that have been reported in critically ill patients have been nausea and vomiting. Fear and anxiety have been described if large doses (more than 10 mg) of flumazenil are given rapidly but

**Table 3.** Details of patients who received an infusion of flumazenil.

| Age (years) | Sex | APACHE (−GCS) | Days sedated | Total dose midazolam (mg) | Flumazenil infusion |
|---|---|---|---|---|---|
| 67 | F | 14 | 4.0 | 50 | 1 mg/hour for 18 hours |
| 78 | M | 9 | 4.0 | 33 | 0.5 mg/hour for 18 hours |
| 22 | M | 11 | 5.0 | 800 | 0.5 mg/hour for 10 days |
| 66 | M | 10 | 0.5 | 20 | 0.5 mg/hour for 8 hours |

these symptoms may represent rapid awakening of the patient in an apparently hostile environment. The apparent safety of flumazenil does not preclude the need for careful dose titration. Adverse cardiovascular responses similar to those seen after naloxone[13] may occur if patients are awakened suddenly with a tracheal tube in place, although this has not been reported to date. Cardiovascular instability has not been reported in studies of reversal of sedation after coronary angiography,[14] but these patients had neither a tracheal tube in place nor a painful surgical incision. The short duration of action of flumazenil (about one hour) may necessitate repeated bolus doses or an infusion in cases of significant benzodiazepine accumulation.

The prolonged benzodiazepine sedation in these patients may be explained by drug accumulation due to the delayed elimination that occurs in the elderly,[15] the critically ill (particularly those with sepsis)[2,3] and a subgroup of the normal population.[4] This is supported by the observation that several of the patients in this study required very small daily doses of midazolam. Alternatives to the use of midazolam are few. Propofol is being investigated currently for this purpose and may prove useful, although we have noticed some haemodynamic instability with this agent, especially in jaundiced patients (unpublished observation). Volatile agents (particularly isoflurane) are also under investigation and may prove useful in the future if the problems of atmospheric pollution and cost are resolved. The exact place of these alternatives compared to the use of midazolam, combined in some patients with the use of the antagonist, remains to be clarified.

The four patients who required a flumazenil infusion needed less than has been calculated theoretically to be necessary (1.44 mg/hour) by Klotz and Kanto.[16] This may indicate that flumazenil, an imidazobenzodiazepine, may be subjected to similar alterations in elimination to those demonstrated for midazolam.[2-4,15]

The patients who did not show an improvement of conscious level after flumazenil are thought to have had other causes for their depressed conscious level including electrolyte abnormalities, tissue hypoxia, cerebral oedema, and hepatic or septic encephalopathy. The last is a poorly understood condition.[17] All made a full neurological recovery except for one patient who had a hepatic resection and died of liver failure.

Anecdotal reports have suggested that flumazenil may reverse some features of hepatic encephalopathy, mediated via the GABA system;[18] further studies are in progress to evaluate its value in this condition. Two patients who responded to flumazenil had undergone liver transplantation but none of their laboratory investigations supported the development of liver failure, and the improvement in conscious level is thought to be due to reversal of residual effects of midazolam.

Sudden awakening may occur, and result in sudden discomfort, when flumazenil is used in patients who have a tracheal tube in place. This resulted in airway obstruction when the tube was bitten in one of our patients. We were prepared for this eventuality and the addition of isoflurane to the inspired gas resolved the situation rapidly. Not all ventilators have the facility to add vapours to the inspired gas. It may be prudent to have ready a suitable dose of a short acting intravenous anaesthetic agent, such as thiopentone, when a patient whose trachea is intubated is to receive flumazenil. The short action of flumazenil makes it unlikely to be a problem of prolonged duration.

In conclusion, flumazenil appears to be a useful agent for reversal of unexpectedly prolonged benzodiazepine sedation in critically ill patients. The short duration of action of flumazenil necessitates either a continuous intravenous infusion or repeated bolus doses if significant benzodiazepine accumulation has occurred. Other recoverable causes of depression of conscious level must be considered if flumazenil does not reverse sedation.

## *Acknowledgments*

We are grateful to Roche Products for the supply of flumazenil and thank the nursing staff of the Intensive Care Unit for their help with this study.

## *References*

1. Crevoisier C, Ziegler WH, Eckert M, Heizmann P. Relationship between plasma concentration and effect of midazolam after oral and intravenous administration. *British Journal of Clinical Pharmacology* 1983; **16**: 51S–61S.
2. Byatt CM, Lewis LD, Dawling S, Cochrane GM. Accumulation of midazolam after repeated dosage in patients receiving mechanical ventilation in an intensive care unit. *British Medical Journal* 1984; **289**: 799–800.
3. Shelly MP, Mendel L, Park GR. Failure of critically ill patients to metabolise midazolam. *Anaesthesia* 1987; **42**: 619–26.
4. Dundee JW, Collier PS, Carlisle RJT, Harper KW. Prolonged midazolam elimination half-life. *British Journal of Clinical Pharmacology* 1986; **21**: 425–9.
5. Ball M, McQuay HJ, Moore RA, Allen MC, Fisher A, Sear J. Renal failure and the use of morphine in intensive care. *Lancet* 1985; **1**: 784–6.
6. Osborne RJ, Joel SP, Slevin ML. Morphine intoxication in renal failure: the role of morphine-6-glucuronide. *British Medical Journal* 1986; **292**: 1548–9.
7. Shelly MP, Cory EP, Park GR. Pharmacokinetics of morphine in two children before and after liver transplantation. *British Journal of Anaesthesia* 1986; **58**: 1218–23.
8. Knaus WA, Draper EA, Wagner DP, Zimmerman JP. APACHE II: a severity of disease classification system. *Critical Care Medicine* 1985; **13**: 818–29.
9. Park GR, Shelly MP, Manara AR, Quinn K. Sedation in intensive care: morphine and renal failure. *Intensive Care Medicine* 1987; **13**: 365–7.
10. Ramsay MAE, Savege TM, Simpson BRJ, Goodwin R. Controlled sedation with alphaxolone–alphadolone. *British Medical Journal* 1974; **2**: 656–9.
11. Bodenham A, Brownlie G, Dixon JS, Park GR. Reversal of sedation by prolonged infusion of flumazenil. *Anaesthesia* 1988; **43**: 376–8.
12. Kleiberger G, Grimm G, Laggner A, Druml W, Lenz K, Schneeweiss B. Weaning patients from mechanical ventilation by benzodiazepine antagonist RO 15-1788. *Lancet* 1985; **ii**: 268–9.
13. Pinnock CA, Smith G. Naloxone—paradox or panacea? *British Journal of Anaesthesia* 1985; **57**: 547–9.
14. Geller E, Chernilas J, Halpern P, Niv D, Miller HI. Hemodynamics following reversal of benzodiazepine sedation with RO 15-1788 in cardiac patients. *Anesthesiology* 1986; **65**: A49.
15. Harper KW, Collier PS, Dundee JW, Elliott P, Halliday NJ, Lowry KG. Age and nature of operation influence the pharmacokinetics of midazolam. *British Journal of Anaesthesia* 1985; **57**: 866–71.
16. Klotz U, Kanto J. Pharmacokinetics and clinical use of flumazenil (RO 15-1788). *Clinical Pharmacokinetics* 1988; **14**: 1–12.
17. Hasselgren PO, Fischer JE. Septic encephalopathy. Etiology and management. *Intensive Care Medicine* 1986; **12**: 13–6.
18. Mullen KD, Martin JV, Mendleson WB, Bassett ML, Jones EA. Could an endogenous benzodiazepine ligand contribute to hepatic encephalopathy? *Lancet* 1988; **I**: 457–9.

*Anaesthesia*, 1989, Volume 44, pages 606–607

SPECIAL ARTICLE

# Anaesthesia and the law

## Monitoring

D. Brahams, Barrister-at-Law, 5 New Square, Lincoln's Inn, London WC2A 3RJ.

Arguably, many deaths and injuries from hypoxia could be avoided if more comprehensive monitoring equipment and stricter standards of care were imposed on anaesthetists. Those health authorities and private hospitals and clinics who plead lack of cash as justification for operating with outmoded and inadequate equipment and a shortage of trained staff should think again. Leaving aside the human tragedy of an anaesthetic injury or death, one large legal claim for damages can cost more money than ever could be saved by shortsighted economies. Having said that, it is clear that limited cash resources must make for difficult choices; the provision of a new ECG monitor or pulse oximeter, for example, may deprive other departments of valuable equipment and staff or reduce the number of treatments given and so forth.

In Massachusetts, USA, stricter practice standards for anaesthetists are paying off financially. Since these have been in force claims have dramatically reduced and lower premiums are the order of the day, with more reductions planned if the trend continues. Anaesthesia will become a low risk specialty for insurers.[1] In New York State, regulations are being proposed that will require specific monitoring devices to be used during anaesthesia. Further, and in response to the Libby Zion case,[2] there are hopes that maximum hours of work per week will be imposed on junior hospital doctors in New York State in the hope of reducing medical misadventures occurring as a result of fatigue. Though there is much concern about fatigue and long hours in Britain, attempts to legislate in Britain seem doomed to fail.

Similarly, recommendations for stricter standards in anaesthesia remain counsels of perfection with no mandatory force as, for example, suggestions that ECG monitoring should be performed during all routine anaesthesia.[3] The Association of Anaesthetists of Great Britain and Ireland has published recommended standards of monitoring (1988); but, again, these standards do not have the force of law and are not uniformly complied with across the country.

Following an anaesthetic disaster can the plaintiff or his family claim that a failure to follow such recommendations was negligent and caused the injury? In my view, though such guidelines would be persuasive, noncompliance (often through lack of resources) would not necessarily render the anaesthetist or his hospital negligent and it would depend on all the circumstances. The law requires a doctor to be reasonably competent and to provide a reasonable standard of care which may not be optimum. Thus, if the doctor can satisfy the court that he (or she) has complied with a practice considered proper by a responsible body of medical opinion in his field and that he provided a reasonable standard of care to the patient he will not be found negligent.[4]

However, on 9 November 1988, following a Fatal Accident Inquiry into a death arising from dental anaesthesia, a Scottish Sheriff recommended that 'urgent anxious and careful consideration be given by the Authorities to the adoption' of ECG monitoring and the attendance of a state registered nurse trained in resuscitation techniques 'in every case where a general anaesthetic is administered in a dental clinic or a dental surgery'.

In that case an 11-year-old girl was given nitrous oxide, oxygen and halothane by a trained anaesthetist to allow for extraction of four teeth. A standard inhalation technique was used. After the third tooth had been extracted the halothane was stopped and after removal of the fourth tooth the mask was taken off. The child was still breathing easily but then her breathing became shallow and intermittent. The anaesthetist tipped her chair back, gave oxygen via a facemask and rubbed her sternum. This caused an intake of breath but no movement. Her pulse became weaker and he tilted the chair so that her head was below her feet; she was breathing shallowly. She was placed on the floor, breathing intermittently from the oxygen mask but with no pulse.

The anaesthetist then requested a defibrillator from the recovery room and an ECG trace confirmed that the child had suffered a cardiac arrest. The trace showed ventricular fibrillation. He then inserted a Brook airway and the dentist performed expired air resuscitation. The anaesthetist believed there was sufficient oxygenation of the patient to permit defibrillation but he was unable to restore the heart rhythm, and after the first application asystole occurred. Cardiac massage and lignocaine produced a very slow heart trace three times but breathing could not be maintained and the patient died 2 days later in hospital.

The sheriff determined that the child's death might have been avoided if an electrocardiograph had been used to monitor her heart, a state registered nurse trained in resuscitation techniques had been in attendance, and if the patient's trachea had been intubated and her lungs ventilated using a tracheal tube with 100% oxygen immediately cardiac arrest had been diagnosed. (At the inquiry, the anaesthetist was criticised by the sheriff's medical expert for failing to intubate promptly and that this should have been his first priority rather than defibrillation.)

The sheriff said that 'the most significant evidence in the inquiry was the ready acceptance that acute cardiac failure can occur during dental anaesthesia even when an impeccable anaesthetic technique is employed by an experienced anaesthetist. Anyone who has teeth extracted under general anaesthetic is at risk. In these circumstances a requirement to resuscitate a patient is to be anticipated. Adequate personnel and equipment should be on hand to maximise the possibility of a successful resuscitation.' The anaesthetist had the greatest difficulty in carrying out the resuscitation attempt in the absence of skilled assistance as three procedures were required immediately and he could not carry them out by himself at the same time.

Another significant piece of medical evidence given to

0003–2409/89/070606+02 ©1989 The Association of Anaesthetists of Gt Britian and Ireland

the inquiry was that dental anaesthesia in Britain was in an evolutionary state at present and was perhaps 10 years behind North America!

*References*

1. McGinn PR. Practice standards leading to premium reductions. *American Medical News* 2 December 1988.
2. Brahams D. Excessive hours of work. *Lancet* 1988; **ii:** 56–7.
3. Lunn JN, Mushin WW. Mortality associated with anaesthesia: Nuffield Provincial Hospitals Trusts, 1982: 48.
4. Bolam v Friern Hospital Management Committee [1957] 1 WLR 582; see also Brahams D. Dosage of gentamicin and monitoring of blood levels: an action fails; Vernon v Bloomsbury HA. *Lancet* 1986; **1:** 1395–6.

*Anaesthesia*, 1989, Volume 44, pages 608–620

# Correspondence

**Vegetative survival** 608
*S.Q.M. Tighe, FFARCS and C.R.G. Reid, FFARCS*
*B. Jennett, MD, FRCS* 609
**Inadvertent epidural midazolam and fentanyl** 609
*C.S. Goodchild, PhD, FFARCS, J.P. Gent, MA, PhD, R.L. Marks, FFARCS and J.M. Serrao, FFARCS*
**IgA nephropathy and the anaesthetist** 610
*L. Vella, FFARCS*
**Ischaemic lesions related to pressure from the bindings of a wrist splint and cardiopulmonary bypass** 610
*F. Luscombe, FFARCS, A. Teasdale, MB, ChB, and J. Powell, DRCOG DA*
**Intra-ocular pressure and rapid sequence induction of anaesthesia** 611
*R.K. Mirakhur, MD, PhD, FFARCS*
*L. Edmondson, FFARCS, S.L. Lindsay, FFARCS and H.E.R. Chew, DRCOG, FFARCS* 612
**Porphyria and propofol** 612
*P.N. Meissner, BSc, R.J. Hift, MB, ChB, FCP(SA), and G.G. Harrison, MD, FFARCS*
*D. G. Moyes, FFARCS(SA)* 613
*B. Hodkinson, BSc, FFARCS* 613
**Respiratory arrest and retrobulbar block** 614
*D. Crawford, MRCP, FFARCS*
**Sinus arrest after alfentanil and suxamethonium** 614
*C. Ananthanarayan, MD, FRCP*
**Eisenmenger's syndrome and epidural anaesthesia** 614
*D.N. Stokes, MRCP, FFARCS*
*J.C. Sugden, FFARCS and D.S. Selsby, FFARCS*
**Postoperative mediastinal emphysema: blame the anaesthetist?** 615
*P.S. Myles, DRACOG, DA*
**Unusual complication of nasopharyngeal intubation** 615
*W.D. Smith, FFARCS, M.S. Timms, FRCS, and H. Sutcliffe, MSc*
**Use of the Brain laryngeal mask in balanced regional anaesthesia** 616
*L. Murdoch, FFARCS and A. Rubin, FFARCS*
**Controlled ventilation and the laryngeal mask** 616
*J.E. Hammond, FFARCS*
**Pain after laparoscopic sterilisation** 617
*F. Luscombe, FFARCS*
**Second report from an Anaesthetic Reactions Advisory Service** 617
*J.A.W. Wildsmith, MD, FCAnaes*
*J. Watkins, PhD* 617
**Painful injection of propofol** 618
*J.E. Whitlock, FFARCS, M.E. Nicol, FFARCS, J. Pattison, FFARCS*
**A stand for a defibrillator** 618
*M.J. Clancy, FRCS*
**General anaesthesia and presence of the spouse** 618
*R. Freeman, FFARCS, S. Shiva, MB, BS, MD, DA, K. Arunasalam, DA, FFARCS and B.J. Burbridge, FFARCS*
**The ethics of difficult intubation—elective tracheostomy** 619
*I.T. Campbell, MD, FFARCS*
**Apparent resistance to thiopentone** 619
*L.J. Andrew, FFARCS, E.H.S. Yau, MB, BS, and S. Ward, FFARCS*
**Not necessarily a finger on the pulse** 619
*M.R. Nott, DA, FFARCS*
**Cordless 'phones** 620
*J.R. Davies, FFARCS*

## Vegetative survival

In his editorial Professor Jennett states that most hypoxic insults occur in hospital, often under anaesthesia. (*Anaesthesia* 1988; **43:** 921–2). On what evidence is this statement based? We are of the opinion that the majority of such incidents occur on the wards, in the casualty department, or before hospital admission, commonly as a result of cardiac or respiratory arrest. It is further stated that 70% of claims for brain damage are associated with anaesthesia. It should be made clear that this does not mean that 70% of all brain damage is associated with anaesthesia; the relatives of a previously fit patient who has suffered brain damage after elective anaesthesia, a rare event, are far more likely to seek legal redress than the dependants of an individual who has arrived comatose in casualty after a myocardial infarction, a common event.

There were more than 20 000 general anaesthetics administered in 1988 in the Royal Infirmary, Glasgow, but there were no peri-operative deaths or admissions to the intensive care unit after hypoxic–ischaemic brain injury as a result of anaesthesia for noncardiac surgery. A high risk/benefit ratio has usually been clearly appreciated by all concerned prior to the rare occasions that cerebral damage has been associated with anaesthesia. Any cerebral damage that resulted was just as likely to have been caused by the surgery as by the anaesthesia. The recent enquiry into peri-operative deaths has highlighted the contribution of surgery to 30-day mortality in this respect,[1] and so it is not unreasonable to assume that morbidity is similarly related.

The use of the word 'often' is therefore considered inappropriate and unsupported.

---

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in the Notice to Contributors to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision. *If the letter comments on a published article in Anaesthesia, please send three copies; otherwise two copies of your letter will suffice.*

Professor Jennett does not seem to answer the question that he poses, 'can anaesthetists reduce the frequency of a fate worse than death?' He suggests that anaesthetists base their management on prognostic indices that identify patients likely to make a reasonable recovery. This is not helpful, because there is no consensus as to what statistical level can be considererd 'likely', what neurological outcome is 'reasonable', what 'prognostic index' is reliable in these terms and whether conventional levels of statistical significance are relevant at all in this life and death situation. The prognostic indices suggested by the Anglo-American study are impressive,[2] but they are based on the identification of only 25 patients (12%) who survived to an independent state after hypoxic–ischaemic injury, and the authors themselves urge caution in the clinical interpretation of their results. The severely brain damaged group were in addition defined as those patients who retained cognition, but remained dependent on others. This state does not necessarily imply an unreasonable recovery.

The above questions have not been answered by Professor Jennet or anybody else, so there is really no alternative but to continue management on moral, ethical and legal grounds, despite the agony of a fate worse than death.

*The Royal Infirmary,*
*Glasgow G31 3ER*
S.Q.M. Tighe
C.R.G. Reid

### *References*

1. Buck N, Devlin HB, Lunn JN. *The report of a confidential enquiry into perioperative deaths.* London: The Nuffield Provincial Hospital Trust and The King's Fund, 1987.
2. Levy DE, Bates D, Caronna JJ, Cartlidge NEF, Knill-Jones RP, Lapinski H, Singer BH, Shaw DA, Plum F. Prognosis in nontraumatic coma. *Annals of Internal Medicine* 1981; **94:** 293–301.

### *A reply*

It is a pleasure to have the opportunity to clarify points in my editorial which have been misunderstood.

In stating that most hypoxic insults occur in hosptial I was referring to those that progress to vegetative survival. It is when such events occur in hospital that resuscitation is rapidly available, unhappily in time only to save the brain stem but not the cerebral cortex in these cases. Such resuscitation is most easily applied when patients are undergoing some medical intervention with or without anaesthesia. Five spontaneous causes of systemic hypoxic–ischaemic events were listed and I stated that it was almost impossible to discover how often vegetative survival resulted from these. In the absence of audit of near-misses during interventions I suggested that the only evidence available is that from claims. The data I quoted came from the two UK defence organisations and they were consulted about my text before publication.

Severe brain damage as a result of anaesthetic mishaps occurs relatively seldom, but the available figures indicate that it is not rare. Moreover these must underestimate the true incidence because not every such incident results in a claim. The frequency of these occurrences is also underestimated by enquiries into deaths within 30 days. Many such deaths are due to the progress of severe primary disease, and surgery is certainly a factor in a number of these. Surgery probably contributes less often to the particular circumstances that cause neocortical necrosis. Prolonged vegetative survival most often occurs in previously fit and relatively young patients, because older and high risk patients seldom survive for long after such a severe brain insult.

It is not my intention to imply that decisions about withholding or withdrawing life-sustaining measures from severely brain damaged patients are ever easy; I wished only to open the debate on this issue in this country, at a time when there is so much discussion elsewhere. These discussions question the traditional view of Drs Tighe and Reid that there is no option but to treat all such patients as potentially salvable, because predictions of outcome are uncertain. We, as a contribution to this debate, analysed the views of an international group of neurosurgeons who were asked about the levels of probability of a poor outcome that would lead them to consider limiting treatment for victims of severe brain damage.[1]

*Institute of Neurological Sciences,*
*Glasgow G51 4TF*
B. Jennett

### *Reference*

1. Barlow P, Teasdale G. Prediction of outcome and the management of severe head injuries: the attitudes of neurosurgeons. *Neurosurgery* 1986; **19:** 989–91.

---

## Inadvertent epidural midazolam and fentanyl

We read this report (*Anaesthesia* 1989; **44:** 75) with interest. There is one other report of epidural administration of midazolam in man[1] in which it was used in both postoperative and chronic pain states. Sedation was observed after epidural administration of midazolam; the reductions in analogue pain scores reported may therefore be considered unreliable. In addition, no dermatomal level was reported and thus we are left wondering if there was any spinal component to the analgesia or not.

We draw attention to other related studies in which dermatomal levels of analgesia are reported in animals and man after intrathecal midazolam. It was shown by members of our group that intrathecal midazolam produces spinally mediated analgesia in rats by an action on spinal cord benzodiazepine receptors[2] and that it also produces analgesia in postoperative patients; the analgesia exhibited a dermatomal distribution.[3] Thus the weight of scientific evidence indicates that spinal midazolam is antinociceptive at the spinal cord level and this could be clinically useful.

Stedman and Hammond, in common with most clinical reports of analgesia after epidural or intrathecal drugs, do not give a dermatomal level of block and therefore the effect may be the result of actions of either or both drugs on the brain, rather than on the spinal cord. The occurrence of respiratory depression and drowsiness with hypotension tends to confirm this.

These side effects may be caused by transfer of the drugs to the brain via the cerebrospinal fluid. Such spread of a spinally administered drug will cause very high receptor occupancy in the brain. Naloxone 0.4 mg may not be enough to antagonise the fentanyl effects in these circumstances. This would explain the residual analgesia and perhaps some potentiation of sedation and hypotension caused by the benzodiazepine.

Reversal of the residual sedation and hypotension by flumazenil indicated that these were due, at least in part, to the effect of midazolam. This is surprising because only a total of 2.4 mg midazolam was administered over 2 hours. This is a very small dose compared with that normally administered intravenously or intramuscularly and indicates again that these actions were probably the result of a supraspinal spread of the drug away from the site of application via the cerebrospinal fluid. This would cause a much higher receptor occupancy in the brain than would occur after intravenous administration.

The facts of this case therefore are that all the observed effects of the inadvertent administration of these two drugs epidurally may be explained by supraspinal effects of both drugs. The residual analgesia might have been caused by supraspinal effects of fentanyl that remained after the small dose of naloxone had been administered.

Unlike intrathecal administration (we routinely use a 2-mg bolus intrathecally) epidural administration of midazolam is accompanied by considerable sedation, as the report by Stedman and Hammond confirms. The epidural route may be preferred to the intrathecal route if this sedation can be reversed with small doses of flumazenil but a spinal analgesic block be retained. We recommend that investigators define dermatomal levels of analgesia in order to be sure that they study *spinally mediated* analgesia and not merely a partially reversed supraspinal effect.

*University of Leeds,*
*24 Hyde Terrace,*
*Leeds LS2 9LN*

C.S. GOODCHILD
J.P. GENT

*York District Hospital,*
*York*

R.L. MARKS
J.M. SERRAO

*References*

1. RIGOLI M. Epidural analgesia with benzodiazepines. In: TIENGO M AND COUSINS S, ed. *Pharmacological basis of anesthesiology: clinical pharmacology of new analgesics and anesthetics.* New York: Raven Press, 1983: 69.
2. GOODCHILD CS, SERRAO JM. Intrathecal midazolam in the rat: evidence for spinally-mediated analgesia. *British Journal of Anaesthesia* 1987; **59**: 1563–70.
3. GOODCHILD CS, NOBLE J. The effects of intrathecal midazolam on sympathetic nervous system reflexes in man—a pilot study. *British Journal of Clinical Pharmacology* 1987; **23**: 279–85.

---

## IgA nephropathy and the anaesthetist

This is a report of a case of undiagnosed IgA nephropathy which was mistaken for a massive blood transfusion reaction. A 21-year-old female with spondylometaphyseal dysplasia presented to the orthopaedic service for removal of heterotopic bone formation from both hip joints. History, physical examination and blood investigations were normal before operation, but the urine was noted to be cloudy and urinalysis was positive for protein and haemoglobin. The blood loss during surgery was about 1500 ml and the patient received 2 units of packed red blood cells. Urine output was adequate but somewhat dark throughout the operation; however, one hour afterwards urine output diminished considerably and the urine became darker and almost black in colour. The possibility of a blood transfusion reaction due to incompatibility within the ABO system was raised. However, none of the other classical symptoms such as restlessness, anxiety, flushing, chest pain, tachypnoea, tachycardia and nausea were present and laboratory investigations failed to demonstrate an elevated plasma haemoglobin level or the presence of red cell antibodies. The urine returned to normal colour within 5 days and eventually a diagnosis of IgA nephropathy was made by the renal medical team.

Seventy-six percent of 140 cases of patients studied with IgA nephropathy,[1] presented with episodes of recurrent gross macroscopic haematuria. This typically appeared 48–72 hours after a respiratory tract infection, persisted for less than 3 days and was sometimes accompanied by lumbar pain. The syndrome however is also described after tonsillectomy, vaccination, tooth extraction, violent physical exercise and trauma. Our patient developed the syndrome after surgical trauma. It is therefore to be recommended that IgA nephropathy should be considered in the differential diagnosis of darkly coloured urine in the perioperative period as long as a massive blood transfusion reaction has already been excluded.

*St George's Hospital,*
*London SW17 0QT*

L. VELLA

*Reference*

1. RODICIO JL. Idiopathic IgA nephropathy. *Kidney International* 1984; **25**: 717–29.

---

## Ischaemic lesions related to pressure from the bindings of a wrist splint and cardiopulmonary bypass

A 36-year-old man who weighed 128 kg and suffered from Marfan's syndrome presented for replacement of his aortic valve and root.

A 22-G cannula was placed in the left radial artery before induction of anaesthesia and the wrist was placed in a splint to hold it in an extended position, to prevent occlusion of the arterial trace. The splint was held in place by two pieces of 2 cm Velcro tape secured across the forearm and palm and then on to the splint itself, as is our normal practice.

The positioning of the patient was not easy due to his bulk but a satisfactory result with protection of pressure points on the arms and lower limbs was eventually achieved. The operation was not technically easy and the perfusion time was 119 minutes. The mean radial artery blood pressure varied from 40 mmHg to 110 mmHg. The patient bled from the aortic suture line after bypass and haemostasis was only achieved after a further 180 minutes. The blood pressure was pharmacologically held at about 90 mmHg and the patient's lungs were ventilated electively for 12 hours.

The patient complained of intense pain in the left hand after extubation, and on examination the tape across the palm had cut into the flesh below the index finger and below the little finger. There was no motor deficit but some limitation of movement due to pain and swelling. There were separate lesions on the skin, the one across the base of the index finger measured 3 cm in length, and the other

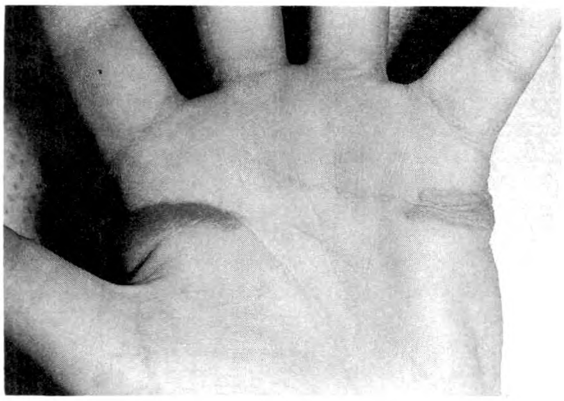


**Fig. 1**

below the little finger 1 cm. These lesions were inflamed and indurated. There were paraesthesiae on the medial border of the little finger and lateral border of the index finger, presumably due to neuropraxia of the digital nerves.

The finger movement returned to normal over the next few days, oedema subsided and the paraesthesiae on the little finger resolved, whilst that of the index finger started to improve. The skin is healing but may leave a scar below the index finger.

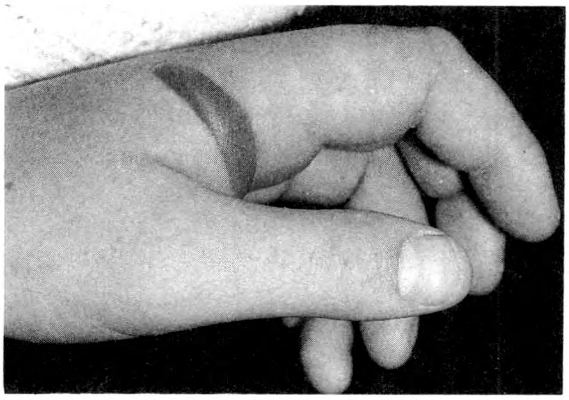


**Fig. 2**

This case illustrates the need not only to protect pressure points but also emphasises that prolonged periods of relative hypotension, as in cardiopulmonary bypass, may exacerbate the ischaemic effect of pressure.

*Southampton General Hospital,*
*Southampton SO9 4XY*

F. Luscombe
A. Teasdale
J. Powell

---

## Intra-ocular pressure and rapid sequence induction of anaesthesia

The conclusion by Dr Edmondson and colleagues (*Anaesthesia* 1988; **43:** 1005–10) that the use of suxamethonium as part of a rapid sequence induction technique results in good stability of intra-ocular pressure (IOP) deserves some comment.

Observation of no significant change in IOP after the thiopentone–suxamethonium induction sequence in their study is the net result of a reduction in IOP with thiopentone and an increase after suxamethonium as we demonstrated.[1] Edmondson *et al.* would have observed this sequence had they measured the IOP after thiopentone but before suxamethonium administration. The reduction in IOP due to thiopentone is clearly demonstrated in Group B in their study since atracurium produces no significant change in IOP.[2,3] The practical importance of this is in the interpretation of IOP in a perforated eye. The IOP in a perforated eye is essentially atmospheric or zero. Any manoeuvre, such as administration of suxamethonium or tracheal intubation, always results in an increase in IOP.

The work of Lavery *et al.*[3] is quoted somewhat out of its proper context. Lavery *et al.* did not recommend suxamethonium since not only was the postintubation IOP 3 mmHg higher than the baseline value (a 'statistically significant' increase of about 25%) but the increase was more than twice that when compared to the value before intubation. The IOP never exceeded the baseline value in the atracurium group, however, and the increase after intubation was considerably less than in the suxamethonium group. It was on this basis that Lavery *et al.* recommended the use of atracurium for use in rapid sequence induction in patients with perforated eye injuries. These would have been the conclusions of any reasonable observer. We have recently described a technique with vecuronium and propofol which gives the best results in terms of stability of the IOP.[4] Vecuronium and propofol are both preferable to atracurium and thiopentone respectively in terms of a reduction in IOP.[5,6]

The overall technique of induction in a patient with perforated eye injury in whom a rapid sequence induction is required is as important as the individual agents themselves. We do not consider the administration of a muscle relaxant at a variable time of 20–50 seconds before the induction agent as a particular disadvantage. The wide individual variations in the response to muscle relaxants are important and this method ensures that each patient receives the agents at a time that is appropriate. The aim, of course, is to allow as much time as possible between the relaxant administration and intubation and to intubate at the peak effect of the induction agent. The intubation using this technique is carried out within a minute of the patient losing consciousness.

Edmondson *et al.* quote the paper by Libonati and her colleagues[7] in support of stability of the IOP with use of suxamethonium. Libonati *et al.* carried out only a retrospective survey of less than half the cases admitted to their hospital in a given year and they did not measure IOP in any of them. Moreover, their main criterion of success, instead of the quality of visual function, was either the lack of extrusion of the contents of the eye, or as they described 'the description of the eye on the operative report essentially was unchanged from that in the progress note prior to induction of anesthesia'.

A logical analysis of the nature of dynamics in a perforated eye and the effects of drugs used in anaesthesia indicates that the use of suxamethonium is undesirable as part of a rapid sequence technique of induction of anaesthesia.

*Royal Victoria Hospital,*
*Belfast*

R.K. Mirakhur

*References*

1. Mirakhur RK, Shepherd WFI, Darrah WC. Propofol or thiopentone: effects on intraocular pressure associated with induction or anaesthesia and tracheal intubation (facilitated with suxamethonium). *British Journal of Anaesthesia* 1987; **59:** 431–6.

2. Maharaj RJ, Humphrey D, Kaplan N, Kadwa H, Blignaut P, Brock-Utne JG, Welsh N. Effects of atracurium on intraocular pressure. *British Journal of Anaesthesia* 1984; **56**: 459–63.
3. Lavery GG, McGalliard JN, Mirakhur RK, Shepherd WFI. The effects of atracurium on intraocular pressure during steady state anaesthesia and rapid sequence induction: a comparison with succinylcholine. *Canadian Anaesthetists' Society Journal* 1986; **33**: 437–42.
4. Mirakhur RK, Shepherd WFI, Elliott P. Intraocular pressure changes during rapid sequence induction of anaesthesia: comparison of propofol and thiopentone in combination with vecuronium. *British Journal of Anaesthesia* 1988; **60**: 379–83.
5. Mirakhur RK, Shepherd WFI, Lavery GG, Elliott P. The effects of vecuronium on intra-ocular pressure. *Anaesthesia* 1987; **42**: 944–9.
6. Mirakhur RK, Shepherd WFI. Intraocular pressure changes with propofol ('Diprivan'): comparison with thiopentone. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 41–4.
7. Libonati MM, Leady JJ, Ellison N. The use of succinylcholine in open eye surgery. *Anesthesiology* 1985; **62**: 637–40.

### *A reply*

Thank you for the opportunity to reply to Dr Mirakhur's letter.

Suxamethonium raises intra-ocular pressure (IOP) by the production of tonic contractions of the extra-ocular muscles of the eye[1] and causes vasodilatation of blood vessels in the eye.[2] Thiopentone probably lowers IOP by a reduction of choroidal blood volume secondary to a decrease in central venous pressure. Thiopentone also abolishes the tonic contractions of the extra-ocular muscles of the eye seen with suxamethonium.[3] The net effect on the IOP when both are given sequentially is dependent on the timing of their administration. A study of their separate effects on IOP would not elucidate their combined effect on IOP when given rapidly and sequentially in the rapid sequence induction technique. Our study clearly demonstrated the changes in IOP in this situation.

What is the practical importance of our findings in penetrating eye injuries? The IOP of a perforated eye is at atmospheric pressure. Anaesthetic drugs or manoeuvres that raise IOP in the intact eye risk vitreous loss in the perforated eye. It is probably true to say that those agents that cause the greatest increase in IOP in the intact eye have the greatest risk of vitreous extrusion in the perforated eye. Suxamethonium given in isolation produces a mean increase in IOP of 7 mmHg;[4] intubation of 5 to 30 mmHg;[5] and coughing increases of up to 4 mmHg.[6] Our study demonstrated that after rapid administration of adequate doses of thiopentone and suxamethonium as part of a rapid sequence induction and intubation technique, the increase in IOP was a mean of 1 mmHg. This would therefore indicate a relatively low risk of vitreous extrusion.

Dr Mirakhur recommends the administration of non-depolarising muscle relaxants 20 to 50 seconds before induction for patients with penetrating eye injuries who require a rapid sequence induction. This is certainly a more complicated technique than that used with suxamethonium, and although Lavery *et al.*[7] used this technique, and found that after intubation the IOP remained below baseline, other authors[8] were not able to recommend the technique. Mallaiah *et al.* found that IOPs after intubation were higher than baseline and that 50% of patients exhibited slight or severe bucking on intubation. Can we therefore be certain that this technique consistently produces lower IOPs than rapid induction with thiopentone and suxamethonium?

It should also be noted that vitreous extrusion is no longer considered such a disastrous event by ophthalmologists because it is now possible to avoid many of the mechanisms by which vitreous loss further damages the eye.[9,10]

The anaesthetic dilemma is to balance the risks in a patient with a penetrating eye injury and a potentially full stomach. Amongst the risks to be considered are further damage to the eye from vitreous loss, pulmonary aspiration and failure to intubate. The logical analysis of the data now available indicates that the use of suxamethonium as part of a rapid sequence technique of induction of anaesthesia in a patient with a penetrating eye injury, is not as undesirable as previously thought.

*The Children's Hospital,*
*Birmingham B16 8ET*
L. Edmondson
S.L. Lindsay

*21 Tycehurst Hill,*
*Loughton,*
*Essex IG10 1BX*
H.E.R. Chew

*References*

1. Lincoff HA, Ellis CH, De Voe AG, De Beer EJ, Impastato DJ, Berg S, Orkin L, Magda J. The effect of succinylcholine on intraocular pressure. *American Journal of Ophthalmology* 1955; **40**: 501–10.
2. Wahlin A. Clinical and experimental studies on effects of succinylcholine. *Acta Anaesthesiologica Scandinavica* 1960; (Suppl. 5): 1–24.
3. Lincoff HA, Breinin GM, De Voe AG. The effect of succinylcholine on the extraocular muscles. *American Journal of Ophthalmology* 1957; **43**: 440–4.
4. Cook JH. The effect of suxamethonium on intraocular pressure. *Anaesthesia* 1981; **36**: 359–65.
5. Wynands JE, Crowell DE. Intraocular tension in association with succinylcholine and endotracheal intubation: a preliminary report. *Canadian Anaesthetists' Society Journal* 1960; **7**: 39–43.
6. Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *British Journal of Anaesthesia* 1980; **52**: 671–9.
7. Lavery GG, McGalliard JN, Mirakhur RK, Shepherd WFI. The effects of atracurium on intraocular pressure during steady state anaesthesia and rapid sequence induction: a comparison with succinylcholine. *Canadian Anaesthetists' Society Journal* 1986; **33**: 437–42.
8. Mallaiah S, Eltringham RJ, Magauran DM. Atracurium and vecuronium in emergency eye surgery. *Anaesthesia* 1986; **41**: 84–5.
9. LeMay M. Aspects of measurement in ophthalmology. *British Journal of Anaesthesia* 1980; **52**: 655–62.
10. Lichstenstein SB. In: Duane TD, ed. *Clinical ophthalmology*. New York: Harper and Row, 1987: 1–9.

## Porphyria and propofol

Drs Weir and Hodkinson advise against the use of propofol in patients with porphyria (*Anaesthesia* 1988; **43**: 1023–4). We consider that this statement requires qualification.

Firstly, we question whether a finding of 26 $\mu$mol porphobilinogen/24 hours postoperatively is significant in terms of the development of an acute attack of variegate porphyria. The reported excretion of 26 $\mu$mol porphobilinogen/24 hours in our experience would probably not be associated with clinical symptoms, contrary to these

# FLUID RESUSCITATION

(Baillières Clinical Anaesthesiology)

EDITORS: **W. Kox** *Dept Anaesthesia, Charing Cross and Westminster Medical School, London, UK*

**J. Gamble** *Dept Physiology, Charing Cross and Westminster Medical School, London, UK*

THIS practical, research-based reference book not only covers the wide range of topics that need to be addressed during the management of patients in shock, but also considers the rationale for their implementation.

Up-to-date reviews include new approaches in resuscitation, e.g. the development of artificial $O_2$ carriers and the use of low volume hyperosmotic, hyperoncotic resuscitation techniques. The ongoing discussion, crystalloid versus colloid fluid replacement, is considered. The cardiovascular effects of fluid administration as well as the rationale for the use of ionotropic and vasoactive drugs following fluid loading are examined. Likewise, the effect of protein metabolism and fluid balance and its implications on parenteral nutrition during the process of fluid resuscitation is discussed. Problems arising from fluid replacement therapy such as reperfusion injury, the administration of particulate contaminants, plasma substitutes and the interference of these substances with blood grouping are addressed as well as the prevention and treatment of fluid overload. This book caters for the requirements of specialists in intensive care, anaesthetists as well as physicians and surgeons who are interested in understanding and thereby pre-empting shock-related injury.

## Contents

PATHOPHYSIOLOGY AND PRINCIPLES OF FLUID RESUSCITATION:

**J. Gamble** - The principles governing microvasculature transendothelial fluid exchange
**A. Kirkman & R.A. Little** - The pathophysiology of trauma and shock
**S. J. Machin** - Disturbances of haemostasis in surgical and critically ill patients
**M.I.M. Noble** - Cardiovascular response to fluid loading
**J.L. Vincent** - A rationale for the use of inotropic and vasoactive drugs during fluid loading

FLUID REPLACEMENT THERAPY:

**U. Kreimeier & K. Messmer** - Fluid replacement in shock
**W. Shoemaker** - Crystalloid versus colloid fluid resuscitation
**E.S. Parry** - The use of blood products in the treatment of hypovalaemia and shock
**D. Denison** - Artificial oxygen carriers
**A. Fleck** - Nutrition, protein metabolism and fluid balance

SEQUELAE AND SIDE-EFFECTS OF FLUID RESUSCITATION:

**D. Royston** - Reperfusion injury
**W. Kox** - Influence of plasma substitutes on blood typing and cross matching
**H. Hesselvick & B. Brodin** - Reticulo-endothelial response to administration of plasma substitutes
**C.N. McCollum** - The use of microfilters in fluid resuscitation
**T.A. Golper** - Treatment of the overhydrated patient in the ITU

**0 7020 1340 4 ca 230pp Hb June 1989 Baillière Tindall £18.50**

**Baillière Tindall**

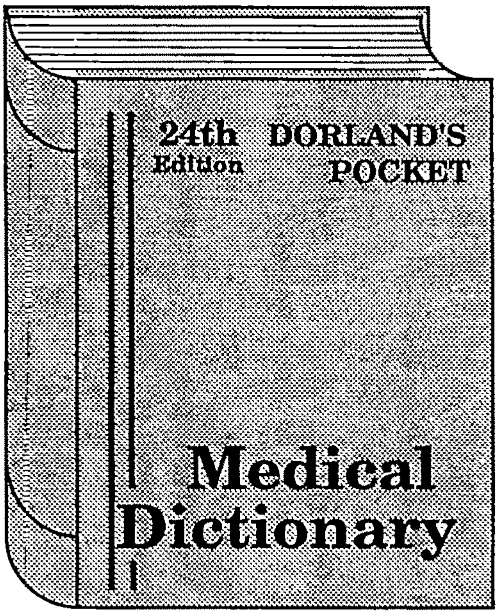
**Available from your local bookseller. Prices, specifications and availability are subject to change without prior notice. For further information please contact: Marketing Department, Harcourt Brace Jovanovich Ltd, 24-28 Oval Road, London NW1 7DX, UK.**

*NOW AVAILABLE FROM*

# W.B. SAUNDERS

## DORLAND'S POCKET MEDICAL DICTIONARY

*24th Edition*



The most current and comprehensive portable medical reference available. For the 24th edition coverage has been expanded to include over 3000 new terms and advances in such areas as AIDS, magnetic resonance imaging and immunology. In keeping with its 40 year history definitions and tables have been revised and updated to reflect current usage. Abridged from *Dorland's Illustrated Medical Dictionary, 27th Edition*, this pocket version is designed to reflect the most frequent needs of users. Thumb indexed and in a durable flexible cover the dictionary should be an essential purchase for health care professionals of every specialty.

## Contents

Preface - Notes on the Use of the Book - Combining Forms in Medical Terminology - Vocabulary - Tables of Arteries - Table of Bones, Listed by Regions of the Body - Table of Bones - Table of Chemical Elements - Human Immunoglobulin Classes - The Human Body: Highlights of Structure and Function (*containing 16 colour plates*) - Table of Muscles - Table of Nerves - Positioning of the Fetus in Various Presentations - Table of Temperature Equivalents - SI Units - Prefixes for SI Units - Table of Veins - Table of Weights and Measures.

**0 7216 2202 X 688 pp Ills Flexible cover January 1989 W.B. Saunders £12.50**

---

**Available from your local bookseller. Prices, specifications and availability are subject to change without prior notice. For further details please contact: Marketing Department, Harcourt Brace Jovanovich, 24-28 Oval Road, London NW1 7DX, UK.**

W.B. Saunders Baillière Tindall
HARCOURT BRACE JOVANOVICH

authors. The upper limit of 'normal' porphobilinogen excretion is usually quoted in the region of 15,[1] not 9 μmol/24 hours, and the acute attack of variegate porphyria is associated with far higher porphobilinogen levels than the small increase reported here. In an analysis of 10 acute attacks of variegate porphyria the mean urinary porphobilinogen levels were found to be 290 μmol/day (range 64–587) and normal levels were given as < 22 μmol/day.[2] An earlier analysis of 60 acute attacks of variegate porphyria found urinary porphobilinogen concentrations to be even higher.[3]

Secondly, and more importantly, we hesitate to conclude that propofol alone was responsible for the porphyrin and porphobilinogen alterations when 60 mg lignocaine was sprayed onto the larynx and this was the patient's third operative procedure in as many days. We too have used lignocaine in similar small doses in porphyric patients without deleterious effects. However, lignocaine is categorised as 'unsafe/dangerous' in most published drug lists[4–6] since it was shown to be an inducer of rat liver 5-aminolaevulinic acid synthase.[7] We do acknowledge that it may be misleading to extrapolate from an animal model to the human, but consider that the potential porphyrinogenicity of lignocaine should have been considered in this case. Furthermore, the cumulative stress of three recent operations may well have contributed towards the increase in porphobilinogen and porphyrins in this patient.

We emphasise even on the assumption that propofol was responsible for these changes, that in this case propofol was used as an infusion in a relatively large dose and that it may be perfectly safe in the smaller doses appropriate for the induction of anaesthesia. It has a short half-life[8] and it appears to be safe in an animal model of porphyria.[9] We have recently monitored porphyrin precursors and porphyrins in 13 variegate porphyric subjects who received propofol (3–4 mg/kg) for induction of anaesthesia. There was no significant increase in any of the parameters measured over the trial period and no patient developed clinical evidence of an acute attack. This study will be submitted for publication shortly.

We thus consider that Drs Weir and Hodkinson's conclusion that propofol is unsafe for use in the porphyric patient is not entirely justified. It may well prove to be an extremely useful induction agent for the anaesthetist confronted with a porphyric patient.

*Liver Research Centre,*
*University of Cape Town,*
*7925 Observatory*
*South Africa*

P.N. Meissner
R.J. Hift
G.G. Harrison

### *References*

1. Moore MR, McColl KEL, Rimington C, Goldberg A. *Diseases of porphyrin metabolism.* New York: Plenum, 1987: 57–9.
2. Day RS, Eales L, Meissner D. Coexistent variegate porphyria and porphyria cutanea tarda. *New England Journal of Medicine* 1982; **307:** 36–41.
3. Eales L, Day RS, Blekkenhorst GH. The clinical and biochemical features of variegate porphyria: an analysis of 300 cases studied at Groote Schuur hospital, Cape Town. *International Journal of Biochemistry* 1980; **12:** 837–53.
4. Disler PB, Blekkenhorst GH, Eales L, Moore MR, Straughan J. Guidelines for prescription in patients with the acute porphyrias. *South African Medical Journal* 1982; **61:** 656–60.
5. Conradie EA, Straughan JL. *South African medicines formulary*, 1st edn. Cape Town: Medical Association of South Africa, 1988: 88–9.
6. Moore MR. International review of drugs in the acute porphyrias. *International Journal of Biochemistry* 1980; **12:** 1089–97.
7. Parikh RK, Moore MR. Effect of certain anaesthetic agents on the activity of rat hepatic δ-aminolaevulinate synthase. *British Journal of Anaesthesia* 1978; **50:** 1099–103.
8. Cockshott ID. Propofol ('Diprivan') pharmacokinetics and metabolism—an overview. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 45–50.
9. Parikh RK, Moore MR. A comparison of the porphyrinogenicity of diisopropylphenol propofol and phenobarbitone. *Biochemical Society Transactions* 1986; **14:** 726–7.

The article of Weir and Hodkinson (*Anaesthesia* 1988; **43:** 1022–3) was read with interest. The increased urinary porphyrins are of concern and it would have been interesting to follow faecal porphyrin production. There is little doubt that in the stable elective variegate porphyric, little reaction may occur even with well known inducers of ALA synthetase. The problem comes with 'unstable' porphyrics particularly during pregnancy. Meanwhile, I agree with the authors and advocate caution until results of the rat model tests and liver cell tests are to hand. The stakes are high and treatment of a porphyric crisis is still not guaranteed to result in survival.

*Baragwanath Hospital,*
*University of Witwatersand,*
*2193 South Africa*

D.G. Moyes

### *A reply*

The reference range used by our laboratory here gives an upper limit of normal for 24-hour porphobilinogen of 9 μmol. The increased porphobilinogen to 26 μmol/24 hours was accompanied by uroporphyrin level at nearly seven times the normal and coproporphyrin level of five times the normal. These increased levels were not accompanied by any symptoms and we did not intend to give the impression that this patient had experienced an acute attack.

The matter of lignocaine as a porphyrinogenic drug was considered in a previous letter (*Anaesthesia* 1989; **44:** 532). Meissner *et al.* do themselves state that small doses of lignocaine would not be expected to have any deleterious effects. This was indeed the third operative procedure in a short period of time, so we did take a urine sample immediately before the propofol infusion. The porphyrin screen on this sample was normal despite all his previous surgery.

Dr Moyes and I agree about the use of propofol in known porphyrics; other factors are always present if propofol is used for surgical procedures and may obscure the issue. Perhaps 60 mg lignocaine used topically was the culprit but I doubt it. However, a patient with known variegate porphyria was given a 50-minute infusion of propofol to a total dose of 900 mg and subsequently showed marked elevation of urinary porphyrins. We must await the results of further study before giving propofol a clean bill of health in porphyria.

*Auckland Hospital,*
*Auckland,*
*New Zealand*

B. Hodkinson

## Respiratory arrest and retrobulbar block

The report of Drs Rigg and James, (*Anaesthesia* 1989; **44:** 26–7) of two cases of respiratory arrest after retrobulbar block was interesting since I was recently in the cardiac arrest team called to the local eye hospital to resuscitate a 78-year-old woman. She had ischaemic heart disease, aortic stenosis and controlled congestive failure and had been scheduled for elective cataract surgery under local anaesthesia. Oral premedication with 2 mg diazepam and topical cyclopentolate and phenylephrine eye drops were followed by a retrobulbar block using 4 ml of a mixture of 2% lignocaine with adrenaline and 0.5% bupivacaine with adrenaline performed on the ward. A further 1.5 ml of local anaesthetic were used to block the superior rectus and facial nerve (Van Lint method). Three minutes later she was unresponsive, cyanosed and apnoeic. The trachea was intubated by the ophthalmologist and her lungs ventilated for 10 minutes before spontaneous ventilation returned. She was awake, frightened with good colour and normal pulse and blood pressure when the resuscitation team arrived. She was taken to the Coronary Care Unit at this hospital but serial cardiac enzymes and ECGs did not reveal any fresh myocardial ischaemia. There was a similar episode in another hospital in this district this year. Published data suggest that local anaesthetic appears in the subdural space in 2%[1] of retrobulbar blocks and that respiratory arrest occurs in 0.3%.[2] It seems that these blocks should only be performed with an intravenous cannula in place and full resuscitation facilities immediately to hand and that after retrobulbar injection all patients should be observed constantly.

*Newcastle General Hospital,*
*Newcastle upon Tyne NE4 6BE*

D. Crawford

*References*

1. Lombardi G. Radiology in neuro-ophthalmology. Baltimore: Williams and Williams, 1967: 6–8.
2. Wittpenn JR, Rapoza P, Sternberg P, Kuwashima L, Saklad J, Patz A. Respiratory arrest following retrobulbar anesthesia. *Ophthalmology* 1986; **93:** 867–70.

## Sinus arrest after alfentanil and suxamethonium

Sinus arrests are reported after suxamethonium in conjunction with narcotics. This is a report of a patient who had a sinus arrest for 20 seconds after induction.

A 35-year-old healthy woman had a laparoscopic investigation for infertility as an outpatient.

The patient was given 10 mg gallamine, 500 µg alfentanil and 500 µg droperidol. She was asked to breathe 100% $O_2$ via a facemask and induction was with 300 mg thiopentone followed by 100 mg suxamethonium. Her lungs were ventilated with 100% $O_2$ by mask. Ten seconds later she was bradycardic to a rate of 20/minute from 100 beats/minute; the ECG then showed asystole and she had no heart sounds and no blood pressure. Immediately two precordial thumps were given while an assistant gave 0.2 mg glycopyrronium and ventilation by mask was maintained. It took 20 seconds for the heart to restart. The trachea was intubated and her blood pressure returned to 110/70 mmHg and her heart rate to 100/minute after resuscitation. The rest of the procedure and surgery was uneventful.

Vagally mediated bradycardia and sinus arrests occur frequently with large doses of potent narcotics, such as fentanyl and its derivatives.[1,2] Sinus arrests or bradycardia and asystole are reported when suxamethonium is used with alfentanil[3,4] or with sufentanil.[5]

Defasciculant doses of gallamine may result in a decrease in bradycardia and rigidity after narcotic administration. This report highlights the fact that even with small doses of alfentanil, small doses of defasciculant do not provide total protection against bradycardia. Hence, it may be desirable to give glycopyrronium or atropine at induction.

Another similar case occurred since I wrote this report.

*Mount Sinai Hospital,*
*Toronto,*
*Canada M5G 1XS*

C. Ananthanarayan

*References*

1. Nauta J, De Lange S, Koopman D, Spierdijk J, Van Kleef J, Stanley TH. Anesthetic induction with alfentanil: a new short-acting narcotic analgesic. *Anesthesia and Analgesia* 1982; **61:** 267–72.
2. Sebel PS, Boville JG, Van der Haven A. Cardiovascular effects of alfentanil anaesthesia. *British Journal of Anaesthesia* 1982; **54:** 1185–90.
3. Maryniak JK, Bishop VA. Sinus arrest after alfentanil. *British Journal of Anaesthesia* 1987; **59:** 390–1.
4. Rivard JC, Lebovitz PW. Bradycardia after alfentanil—succinylcholine. *Anesthesia and Analgesia* 1988; **67:** 907.
5. Sherman EP, Lebowitz PW, Street WC. Bradycardia following sufentanil–succinylcholine. *Anesthesiology* 1987; **66:** 106.

## Eisenmenger's syndrome and epidural anaesthesia

Drs Selsby and Sugden (*Anaesthesia* 1989; **44:** 130–2) describe the successful anaesthetic management of a patient with Eisenmenger's syndrome who had a bilateral inguinal herniorrhaphy under epidural anaesthesia. The technique of administration of epidural anaesthesia in such cases must be meticulous and two aspects merit comment.

Firstly, the authors failed to state the method by which the epidural space was located. Using the technique of loss of resistance to air, 40% incidence of air embolism was detected using a Doppler flow probe situated over the right atrium.[1,2] Air embolism was even detected in one patient when the hanging drop method was used to identify the epidural space. Paradoxical embolism of even small amounts of air can result in tissue infarction in vital organs. Adequate hydration with a preloading volume of crystalloid in excess of 1.5 litres appeared to reduce the risk of air embolism. The recommended method is to use loss of resistance to saline. The bacterial filter and catheter should be flushed as thoroughly as possible to prevent the introduction of air during top-ups.

Secondly, it was stated that after the epidural test dose, 14 ml 0.5% plain bupivacaine were injected. The rate of injection was not stated, but the implication is that this was a bolus dose. The importance of cautious administration of bupivacaine in small, controlled increments to facilitate the gradual onset of sympathetic blockade and the resultant reduction in systemic vascular resistance was highlighted recently in these correspondence columns after the case report by Dr Alderson.[3] This precaution is especially pertinent where a patient with a major cardiac lesion is not being monitored invasively.

Drs Selsby and Sugden may rightly point to the excellent outcome in this case, but the opportunity to make such important educational points should not be missed.

*Queen Elizabeth Hospital,*
*Birmingham B15 2TH*
D.N. STOKES

*References*

1. NAULTY JS, OSTHEIMER GW, DATTA S, KNAPP R, WEISS JB. Incidence of venous air embolism during epidural catheter insertion. *Anesthesiology* 1982; **57**: 410–2.
2. SLEIGH JW, SADDLER JM. Air embolus and epidural anaesthesia (letter). *Anaesthesia* 1986; **41**: 878.
3. ALDERSON JD. Cardiovascular collapse following epidural anaesthesia for Caesarean section in a patient with aortic incompetence. *Anaesthesia* 1987; **42**: 643–5.

*A reply*

Thank you for the opportunity to reply to this letter.

A loss of resistance technique using normal saline was used to locate the epidural space in this patient. The risk of air embolus associated with invasive monitoring was mentioned in our paper, and we assumed that the obvious dangers from the injection of air into a vascular epidural space in a patient with a large ventricular septal defect would be self evident to most readers.

The size of the first dose, 14 ml 0.5% plain bupivacaine, is a point which is open to debate. Dr Alderson's patient weighed 55 kg, was 32 weeks pregnant, and was given a dose of 18 ml 0.5% plain bupivacaine. We considered 14 ml to be a reasonable first dose in a 43-year-old patient who weighs 70 kg and has no intra-abdominal mass. We agree with Dr Stokes that epidural anaesthesia in patients with cardiac disease should be conducted cautiously using incremental doses to extend the block.

*Leeds General Infirmary,*
*Leeds LS1 3EX*
J.C. SUGDEN
D.S. SELSBY

---

## Postoperative mediastinal emphysema: blame the anaesthetist?

A 54-year-old woman, who smoked but was otherwise well, underwent a vaginal hysterectomy under spinal anaesthesia and intravenous sedation.

A clear airway was difficult to maintain until it was corrected with a nasopharyngeal airway. Positive pressure ventilation of the lungs was not required; the nasopharyngeal airway was inserted and removed without any evidence of trauma, and there was no attempt to cannulate neck veins. The operation proceeded uneventfully.

Subcutaneous emphysema was palpable around the neck and upper chest on the second day. A chest X ray showed subcutaneous and mediastinal emphysema; there was no pneumothorax. The lung fields were unremarkable. The surgical team attributed these findings to a complication of anaesthesia, and notified me. The patient was reassured and managed with simple analgesics and supplemental oxygen therapy. She recovered uneventfully.

There are several possible explanations for the origin of the mediastinal gas in this patient.[1,2] Pleural puncture with the 25-G spinal needle is a theoretical possibility, but is excluded by the ease and success of the subarachnoid block. Pharyngeal trauma from the nasopharyngeal airway is unlikely since it was passed easily and there was no trauma. Leakage from the operative site, via the retroperitoneal space, is also unlikely since considerable subatmospheric intrathoracic pressures would be required, and the minor transient respiratory difficulty with this patient was resolved before surgery commenced. Retroperitoneal gas was not present on X ray. There was soft tissue infection with gas-forming organisms but the patient was otherwise well, and she recovered uneventfully. Spontaneous rupture of a marginal alveolus may have occurred during the early phase of anaesthesia associated with the transient respiratory obstruction, but it is more likely to have occurred in the postoperative period. This patient was a chronic smoker, and was prone to productive cough (where intrapleural pressures may exceed 100 mmHg.)

The absence of tracheal intubation, positive pressure ventilation, central venous cannulation and brachial plexus blockade effectively exclude anaesthesia as a direct cause of the above. If any of these procedures were performed then they would most likely be implicated. Future cases of postoperative mediastinal emphysema should be examined closely: anaesthesia is not always to blame.

*Royal Melbourne Hospital,*
*Melbourne,*
*Australia*
P.S. MYLES

*References*

1. NICHOLAS JN. Mediastinal emphysema. *British Journal of Anaesthesia* 1958; **30**: 63–76
2. MUNSELL WP. Pneumomediastinum. A report of 28 cases and review of the literature. *Journal of the American Medical Association* 1967; **202**: 129–33.

---

## Unusual complication of nasopharyngeal intubation

The use of nasopharyngeal tubes has increased in the last few years with the availability of soft latex tubes which are less traumatic than the old red rubber versions. They are increasingly used in outpatient dental anaesthesia[1] as the gradual change to the supine from the sitting position makes the maintenance of a clear airway more difficult. In addition, the medical defence organisations have recently advocated their use in preference to oropharyngeal airways, in order to avoid damage to upper dental crowns or bridgework.[2]

We describe a recent problem after the passage of a nasopharyngeal tube in a 32-year-old female patient. This dislodged a foreign body from the posterior nares into the pharynx where it lay undetected until the end of the anaesthetic. It presented a considerable hazard in this position since it was of the right shape and size to have become impacted in the larynx and thus to obstruct the airway completely.

The foreign body was disc-shaped and measured 1.5 × 0.4 cm. It was encrusted in a hard white material, later found to be mainly calcium phosphate, and covered in mucopus. It was a rhinolith formed around a rubber tyre from a child's (Dinky) toy car.

The patient had reported no symptoms referable to the respiratory tract at the visit before operation and when seen afterwards she had no recollection of the acquisition of this foreign body. The size and shape of the object suggests it was introduced via the mouth rather than the nose, probably in infancy. It is likely that a bout of coughing and gagging resulted in its lodgement in the posterior choana where it lay undetected for the next 30 years.

The dangers were well documented in the days before fibreoptic layngoscopy, when blind nasotracheal intubation was widely practised. Nasal polypi and swollen turbinates may be avulsed[3] and carried onwards via the pharynx into the tracheobronchial tree. The same may also apply to blood clots caused by repeated traumatic attempts at nasal intubation. Pharyngoscopy was thus often recommended after passage of the tube through the nose, and before passage into the trachea, in order that foreign material could be removed.

Our experience highlights the fact that nasopharyngeal tubes should not be used in a totally blind manner either, and that pharyngoscopy should be routine after the passage of these tubes in order to ensure a clear airway.

We recommend that the decision to use a nasopharyngeal tube needs to be made at the pre-operative visit in order that assessment of both nasal airways can be included in the examination. Should nasal intubation be mandatory, and nasal abnormality suspected, an ENT opinion should be sought promptly.

*Manchester Royal Infirmary,*
*Manchester M13 9WL*

W.D. SMITH
M.S. TIMMS
H. SUTCLIFFE

*References*

1. DOCTOR NH. Bilateral nasopharyngeal tubes for outpatient dental anaesthesia. *Anaesthesia* 1977; **32:** 273–6.
2. HARGROVE RL. Dental damage during anaesthesia. *Journal of the Medical Defence Union* 1986; **2:** 19.
3. SCAMMAN FL, BABIN RW. An unusual complication of nasotracheal intubation. *Anesthesiology* 1983; **59:** 352–3.

---

## Use of the Brain laryngeal mask in balanced regional anaesthesia

The debate continues about whether a regional anaesthetic technique should be used with general anaesthesia, or with sedation. However, major surgery under regional anaesthesia usually requires general anaesthesia or heavy sedation, and the latter includes the risk of respiratory depression, airway obstruction, hypoxia and hypercapnia.

Siting regional blocks under general anaesthesia is easier for the patient, especially in children and other anxious patients, or when positioning is difficult or painful. It is usually quicker for the anaesthetist, minimising delay in throughput of patients. The anaesthetist is always concerned about the airway while doing the regional block if a mask anaesthetic is employed.

The advantages of avoiding unnecessary intubation with muscle relaxants are obvious, and there are dangers in placing nerve blocks when the patient is paralysed since valuable warning signs may be masked. The use of a Brain laryngeal mask with light anaesthesia seems an ideal solution in a balanced regional anaesthetic technique. Major surgery, that includes such operations as total hip replacement which may be performed in the lateral position, may be managed in this way with advantage to the patient, anaesthetist and the surgical team. There remains the need for vigilance of the airway, which is not guaranteed completely, and monitoring as for any general anaesthetic.

There is an increased risk of regurgitation in abdominal surgery or in the presence of a full stomach, and since aspiration remains possible past a laryngeal mask, tracheal intubation may still be indicated. We believe that the Brain laryngeal mask has a useful role and should increase the feasibility of balanced regional anaesthesia.

*Royal National Orthopaedic Hospital*
*Stanmore,*
*Middlesex HA7 4LP*

L. MURDOCH
A. RUBIN

---

## Controlled ventilation and the laryngeal mask

The Brain laryngeal mask seems to be sweeping the country or, at least, my part of the country.

It offers apart from convenience of use a potential to reduce anaesthetic-related morbidity and mortality by the provision of an easily obtained unobstructed airway and a possible alternative to tracheal intubation in selected cases. In a recent copy of *Anaesthesia*[1] we are told of two cases of oesophageal intubation which resulted in death and I am sure there are many more problems with intubation that never make the headlines. Time will reveal whether the initial promise is fulfilled as more experience is gained.

There is however, one very strong reservation about these devices. We are shown in the promotional video the use of a nasogastric tube to allow the escape of any gases blown into the stomach during positive pressure ventilation when the mask is used. This is a recipe for disaster. It is common experience that nasogastric tubes may become blocked or kinked and would thus fail to relieve any increased pressure. Paradoxically the use of nasogastric tubes may actually precipitate the problem by making the oesophageal sphincters incompetent[2,3] and thus allow easy passage of air into the stomach and on into the bowel. Perhaps even more worrying is the prospect of regurgitation with increased intragastric pressure and incompetent sphincters; we are told that the mask does not protect against aspiration.

Should we ever be using the laryngeal mask with intermittent positive pressure ventilation? My personal feeling is yes, but not with nasogastric tubes in place, although I have to admit there is no evidence for this statement. Despite my use of the mask during controlled ventilation my surgeons have not yet told me that the stomach appears to be distended. It is a good policy to try to keep the inflation pressure low (say less than 2.0 kPa) to decrease the likelihood of distending the stomach. This can usually be achieved by various means such as smaller tidal volumes, lower inspiratory flow rate, good relaxation and most importantly, good patient selection!

I hope many anaesthetists will try the laryngeal mask since only experience and reporting will help this revolutionary new device to find its correct place amongst our armamentarium.

*East Surrey Hospital,*
*Redhill,*
*Surrey RH1 5RH*

J.E. HAMMOND

*References*

1. BRAHAMS D. Anaesthesia and the law. Two cases of oesophageal intubation. *Anaesthesia* 1989; **44: 64–65.**
2. BARTLETT JG, GORBACH SL. The triple threat of aspiration pneumonia. *Chest* 1975; **68:** 560–6.
3. WYNNE JW, MODELL JH. Respiratory aspiration of stomach contents. *Annals of Internal Medicine* 1977; **87:** 466–74.

## Pain after laparoscopic sterilisation

Dr Chaffé's letter (*Anaesthesia* 1989; **44:** 165–6) was very interesting. My colleagues and I have recently completed a study designed to find a way to provide analgesia for daycase laparoscopic sterilisation and to avoid the use of either peroperative or postoperative opiates and their unpleasant side effects in ambulant patients.

We studied two groups of patients for laparoscopic sterilisation as inpatients. A control group of 24 patients had 10-ml saline instilled per cervix into the fallopian tube, and the other group of 22 patients had 10 ml 0.5% bupivacaine instilled. The trial was double blind.

The control group of 19 patients needed and were given opiate postoperative analgesia, whereas only six out of 22 in the study group received analgesia. This is statistically significant. There was also a statistically significant difference in pain levels (using 10-cm linear analogue scales) at 1 and 2 hours after operation. We suggest that this technique may have a useful role in analgesia for daycase laparoscopic sterilisation.

*Southampton General Hospital,*
*Southampton SO9 4XY*

F. LUSCOMBE

## Second report from an Anaesthetic Reactions Advisory Service

It was interesting to read (*Anaesthesia* 1989; **44:** 157–9) the comments on reports of reactions to local anaesthesia in the second report from NAARAS. Dr Watkins refers to delayed reactions to bupivacaine which, he says'. . . may be indistinguishable clinically from anaphylactoid response'. Dr Watkins should provide further information, as requested previously in your columns (*Anaesthesia* 1988; **43:** 706), about these reactions because they are difficult to understand.

The impression, from the brief comments in this report, is that the 'reaction' referred to was, in fact, systemic hypotension after sympathetic block, but which occurred some time after drug administration. All frequent users of central neural blockade should be aware that hypotension may be delayed and not infrequently occurs at the time that the patient is moved from operating table to bed after the procedure. It is a fine point for argument, but this is really a reaction to nerve block, not to the drug itself as is implied by Dr Watkins. To describe this as an adverse drug reaction is really allowing the anaesthetist to escape from responsibility for proper conduct of the anaesthetic.

If delayed, immunologically mediated, reactions to bupivacaine are being reported to NAARAS, they must be published in full.

*The Royal Infirmary,*
*Edinburgh EH3 9YW*

J.A.W. WILDSMITH

### *A reply*

I agree with Dr Wildsmith's comments about adverse reactions, notably delayed hypotension, which involve local anaesthetics.

The question is, should this Unit provide further information on individual cases? The stumbling block here is the confidentiality we maintain to users of the service; no case is revealed without the reporter's permission. This also applies to discussion of the case with the pharmaceutical company whose products are involved. However, some specific publications have appeared; these are designed to stimulate discussion about situations which some of Dr Wildsmith's peers may have found puzzling. There was for example, an early report of sensitivity to red rubber tubes (this is developing into a lively interest in serious systemic reactions, apparently initiated via the surgeon's rubber gloves), a report on prilocaine-involved reactions in Bier's block and, more recently, on our continuing interest in aggregate anaphylaxis.

Our reports are designed primarily to direct the attention of the anaesthetist to the likely incidence, and the relative incidence, of immediate untoward events which he (she) may expect when these drugs are used in *everyday* anaesthetic practice. NAARAS supplies individual assessment of reaction mechanisms, and possible remedies, only to the requesting anaesthetist. As an immunologist I am not qualified to comment on anaesthetic *practice* and for this I defer to distinguished colleagues in the field for their combined views. Generally, it is impossible to determine whether or not a reaction has an immunological *element* without laboratory analysis.

Finally, while Dr Wildsmith chides me for not having responded to his earlier comments (*Anaesthesia* 1988; **43:** 706), your readers should know that I did telephone him about my (and his) concern about validation of local anaesthetic reactions, and invited him to join the NAARAS advisory panel. Unfortunately, lack of time prevented either of us following this up, but the invitation still stands.

*Royal Hallamshire Hospital,*
*Sheffield S10 2JF*

J. WATKINS

## Painful injection of propofol

It has come to our attention that on a number of occasions patients previously treated with intravenous anticancer chemotherapy exhibit marked pain, both at the site of injection and up the arm on induction with propofol. Pain on injection with propofol is well known.[1,2] Hand veins were used in our patients and seemed of adequate calibre. Lignocaine 1% was added to the propofol before injection. Localised thrombophlebitis is a recognised complication of intravenous anticancer chemotherapy, but longstanding damage to veins is not reported.

We consider that in these patients intravenous induction with thiopentone would be more appropriate. We would be interested to hear other views and have reported this to the Committee on Safety of Medicines.

*St Mary's Hospital,*
*London W2 1NY*
J.E. Whitlock

*The Royal Marsden Hospital,*
*London SW3 6TJ*
M.E. Nicol
J. Pattison

*References*

1. McCollum JSC, Dundee JW. Comparison of induction characteristics of four intravenous anaesthetic agents. *Anaesthesia* 1986; **41:** 995–1000.
2. McCulloch MJ, Lees NW. Assessment and modification of pain on induction with propofol (Diprivan). *Anaesthesia* 1985; **40:** 1117–20.

## A stand for a defibrillator

Monitoring of seriously ill patients during transit within the hospital can be difficult. The defibrillator/ECG monitor is often carried by a nurse, which excludes her from nursing the patient. The ECG screen may only be visible to the person carrying the monitor and therefore recognition of arrhythmias may be delayed. Defibrillation can be difficult in that somebody has to support the machine whilst defibrillation is undertaken. The monitor is heavy and there can be difficulty in passing through doors and into lifts.

The use of a holder which supports the defibrillator/monitor above the patient's feet on a standard hospital trolley (See Fig. 1) allows many of these difficulties to be overcome. The nurse is free for other duties, the screen is visible to more people, arrhythmias can be readily seen and defibrillation rapidly carried out. There is also space on the holder to carry such things as a transfer box, resuscitation fluids or a small oxygen cylinder. Equipment can be safely placed without risk to the patient. This holder has been in use for 6 months within our department and has been well received by both medical and nursing staff. It is not available commercially but the undersigned may be able to help individuals to have the stand manufactured.

*St James's University Hospital,*
*Leeds LS9 7TF*
M.J. Clancy

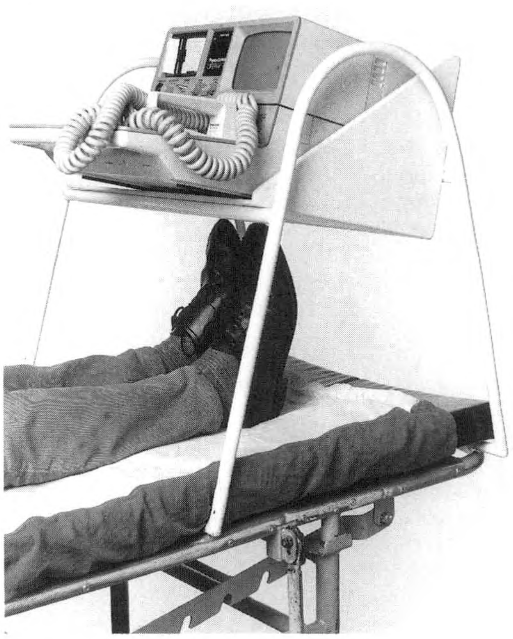


**Fig. 1.**

## General anaesthesia and presence of the spouse

A 26-year-old woman was recently admitted to our Obstetric Unit in labour. She was fit and had delivered two children normally in the past at other hospitals. A letter was in her notes, as is not uncommon in these enlightened times, which requested nursing and medical intervention during her pregnancy only as a very last resort.

The fetus became distressed during the course of labour and immediate lower segment Caesarean section was recommended. She accepted this only on the understanding that the procedure would be performed under general anaesthesia, and that her common law husband would be present throughout.

Somewhat alarmed, the junior obstetricians contacted their consultant who told them to proceed without delay. The junior anaesthetist on call was then summoned to administer the general anaesthetic. Faced with evidence of a deteriorating fetal condition, he decided to continue; the spouse was present throughout. Fortunately the procedure was uneventful.

Whether the junior anaesthetist was correct to continue in these circumstances is a subject of intense debate in this department. We contacted the Medical Defence Union in order to help resolve the issue; they state that an anaesthetist would be expected to do the best he or she could for mother and baby in the circumstances. We were relieved to hear that we could expect full support and assistance from the defence organisations if the spouse interferes with the proper administration of anaesthesia, and harm ensued.

It seems, therefore, that anaesthetists faced with this situation have little option other than to proceed. We are presently formulating a policy with obstetric, nursing, and administrative staff, so that we are in a better position to deal with this situation if it recurs. We would welcome the advice of others who have had similar experiences.

*Wordsley Hospital,*
*Wordsley,*
*West Midlands DY8 5QX*
R. Freeman
S. Shiva
K. Arunasalam
B.J. Burbridge

## The ethics of difficult intubation—elective tracheostomy

This correspondence has horrified me. Would Drs Callander and Thomas (*Anaesthesia* 1988; **43:** 703–4) really subject an otherwise healthy woman to an operation known to carry significant morbidity and even mortality on the grounds than it may help avoid trouble later, when it is by no means certain that problems are inevitable? There are ways other than elective tracheostomy to circumvent them, if difficulties were to arise with their patient. Drs Rice and O'Sullivan (*Anaesthesia* 1989; **44:** 175–6) have already mentioned subarachnoid block; what is wrong with local infiltration or spontaneous ventilation of diethyl ether via a facemask, provided active and positive steps are taken to empty the stomach? Both are perfectly conventional techniques in circumstances, and in parts of the world, where trained anaesthetic help is not available. It must be a very poor reflection on our training system if consultants in this country are unable to use them. The description suggests that this woman's airway was impossible to maintain when she lost consciousness, in which case the suggestion of allowing her to breathe ether spontaneously is irrelevant, but Drs Callander and Thomas do not mention this as a specific problem.

One point that does seem to have escaped them, however, is that although tracheostomy may benefit the respiratory cripple or the patient with upper airways obstruction its value in someone with a normal respiratory tract is less certain. We[1] described a persistent deterioration in arterial oxygenation after major head and neck surgery which involved tracheostomy. Arterial $P_{O_2}$ one week after operation was 2.3 kPa lower than the before operation value, and at one week was showing no sign of recovery. The only cause we could suggest for this persistent hypoxaemia was the presence of the tracheostomy. A tracheostomy has been shown to reduce functional residual capacity[2] in dogs and this is known to impair arterial oxygenation. We suggested the possibility that dry room air which enters the trachea directly would stimulate bronchial secretions, produce reflex bronchoconstriction, narrow the airways and impair gas exchange further. Women in the later stages of pregnancy already have impaired arterial oxygenation mechanisms.[3] A tracheostomy in an otherwise fit, healthy woman might make this impairment worse.

*Royal Liverpool Hospital,*
*P.O. Box 147,*
*Liverpool L69 3BX*

I.T. CAMPBELL

*References*

1. CAMPBELL IT, WILLATT DJ, CHILDS D, STELL PM. Arterial oxygenation after major head and neck surgery involving tracheostomy. *British Journal of Anaesthesia* 1987; **59:** 1121–6.
2. NOGUCH H, TAKUMI Y, ACHI O. A study of humidification in tracheostomised dogs. *British Journal of Anaesthesia* 1973; **45:** 844–8.
3. CRAIG DB, TOOLE MA. Airway closure in pregnancy. *Canadian Anaesthetists Society Journal* 1974; **22:** 665–72.

## Apparent resistance to thiopentone

We report two cases of apparent resistance to sodium thiopentone. Two consecutive patients presented for emergency minor gynaecological procedures. The first patient was aged 23 years and weighed 61 kg. The second was 32 years old and weighed 57 kg. Neither was on any medication nor habituated to alcohol or other drugs. They were not premedicated and both received 0.05 mg fentanyl before induction of anaesthesia. We were surprised that both patients required 30 ml of a 2.5% sodium thiopentone solution to achieve induction of anaesthesia.

Examination of the bottle of sodium thiopentone showed that it was paler in colour compared with another bottle of 2.5% sodium thiopentone. The suspect solution of thiopentone was freshly prepared by the anaesthetist in the usual way, solution of 2.5 g sodium thiopentone (Evans Medical, Batch E801 86A) in 100 ml water for injection.

The suspect bottle was sent to the local Quality Assurance Unit for analysis. A bottle of dry powder from the same batch had 10.6% sodium and 84.87% thiopentone. Our bottle had 5.8% sodium and 44.53% thiopentone. The manufacturers consider that this was an isolated incident.

Apparent resistance to thiopentone may be due to chronic alcoholism; the mechanism is most likely to be cross-tolerance.[1] However, extravasation of thiopentone from a vein proximal to the site of injection was reported to cause radial nerve damage and apparent thiopentone resistance.[2] Awareness during tracheal intubation after induction of anaesthesia with 2.5% sodium thiopentone was suggested to be due to inadequate mixing in a multidose bottle with a resultant concentration gradient.[3]

We suggest that inadequate filling of the multidose bottle with dry power is another unusual and unpredictable cause of apparent resistance to thiopentone.

*Southend Hospital,*
*Essex SS0 0RY*

L.J. ANDREW
E.H.S. YAU
S. WARD

*References*

1. COUDERC E, FERRIER C, HABERER JP, HENZEL D, DUVALDESTIN P. Thiopentone pharmacokinetics in patients with chronic alcoholism. *British Journal of Anaesthesia* 1984; **56:** 1393–7.
2. LEACH AA. An unusual complication of thiopentone administration. *Anaesthesia* 1986; **41:** 762.
3. MACLEOD DM. Awareness during intubation. *Anaesthesia* 1984; **39:** 835–6.

## Not necessarily a finger on the pulse

Hypotension after induction of general anaesthesia and transfer to the orthopaedic operating table, occurring again 24 hours later (*Anaesthesia* 1989, **44:** 170), is indeed unexpected. Continuous manual palpation of the pulse suggested is, however, usually impossible even if it is desirable. Monitoring which can provide a continuous indication of the pulse volume between anaesthetic room and theatre is needed.[1] It should be able to free us from the finger on the pulse. Current ECG or automatic blood pressure measuring instruments are bulky, rely on a mains power supply and are unlikely to be available as free-standing mobile units. Pulse oximetry is not helpful immediately after the use of supplementary oxygen.

Pulse plethysmography has been used since the days of carbon granule transducers.[2] Up-to-date devices can provide useful information about the pulse in a majority of patients. The blood-pressure cuff and an ECG can be applied to every patient in the operating theatre, but a simple, cheap and easy to use pulse monitor is the most practicable device to ensure continuity of care beginning in the anaesthetic room.

*Royal West Sussex Hospital,* M.R. NOTT
*Chichester PO19 4SE*

*References*

1. ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND. *Recommendations for standards of monitoring during anaesthesia and recovery*, 1988: 5.
2. GRIGG KN. 'Right at your finger tips'—is the oximeter only half the story? *Anaesthesia* 1988; **43**: 72–3.

## Cordless 'phones

There is often a conflict, especially out of normal working hours, when an anaesthetist in charge of a patient in the operating theatre is summoned to the 'phone to organise pre- and postoperative care of other patients.

There can be no doubt that it is negligent to leave the anaesthetised patient, except in the care of another trained anaesthetist,[1] yet very few operating theatres have a telephone actually in the operating room. The Survey of Anaesthetic Practice showed that the commonest reason for the anaesthetist leaving the patient is to use the telephone.[2]

The solution, of course, is for the telephone to come to the anaesthetist. 'Cordless' telephones work well indoors, even through several internal walls, and may be brought to the anaesthetist who can continue to observe the patient during the telephone conversation.

We have found these telephones give clear reception and are easy to use. They are cheap, approximately £100, will simply replace any modern 'phone which has a plug in lead, and can be used as an ordinary phone at other times. The radio transmission power is very low and hand set is battery powered, so interference with monitoring and other equipment is most unlikely.

We believe that every suite of operating theatres where emergency anaesthesia is carried out should have at least one cordless 'phone.

*Royal Lancaster Infirmary,* J.A. DAVIES
*Lancaster LA1 4RP*

*Reference*

1. GREEN RA. A matter of vigilance. (Editorial). *Anaesthesia* 1986; **41**: 129–30.
2. Survey of Anaesthetic Practice, Association of Anaesthetists of Great Britain and Ireland, 1988.

*Anaesthesia*, 1989, Volume 44, pages 621–622

# Book reviews

**Baillière's Clinical Anaesthesiology, March 1988: clinical research in anaesthesia** 621
Edited by D.E.F. Newton and N.R. Webster
**Obstetric anaesthesia: the complicated patient, 2nd edn** 621
F.M. James, A. Scott Wheeler and D.M. Dewan
**Manual of drug interactions for anesthesiology** 621
R.A. Mueller and D.B.A. Lundberg
**Books received** 622

## Baillière's Clinical Anaesthesiology, March 1988: clinical research in anaesthesia

Edited by D.E.F. Newton and N.R. Webster. Pp. ix + 241. Baillière Tindall, 1988. £15.00.

This, on the face of it, is a book that nice people should not read. It is an introduction to research in (clinical) anaesthesia. The title says that it is about *Clinical Research in Anaesthesia* but it cannot be since there are, for example, a very useful chapter on animal experimentation and the statutory pieces on statistical analysis and computers.

Once into the book, I could easily imagine the tyro with this volume in one hand and the controls of a measuring instrument in the other. Is that really how it is done? The writer of the introduction, on the 'way into research' does not think so. Most young researchers have ready access to expert opinions on a good deal of the commonly used methodologies of anaesthetic research.

Many of the failed projects, or failed reports, result from inadequate use of that opportunity. Perhaps the tyro could eyeball the expert more confidently after a night or two of prior reading if there is a backwardness in this. If, perchance, I am anything of an expert I can only say that I have yet to meet such a well prepared individual.

For my limited circle of not completely nice people, however, I reckon that this book will appeal for its useful update on clinical measurement techniques, with special emphasis on cardiovascular, respiratory, neuromuscular and pain relief methodology. Unfortunately, in my own case it is too late to say that I will not be reading it, but I shall keep it for its comprehensive and up-to-date bibliography, and as a memento of the distinguished and fluent writers that the editors have managed to persuade.

A.A. Spence

## Obstetric anaesthesia: the complicated patient, 2nd edn

F.M. James, A. Scott Wheeler and D.M. Dewan. Pp. 477. Quest-Meridien, 1988. $98.75.

The second edition of this book is welcome; it continues the successful formula of the first, but with the addition of 12 new chapters. The majority of obstetric textbooks adopt an almost uniform format, with the mother as the central figure in each chapter; they usually start with an outline of the physiological changes of pregnancy and progress to anaesthesia and analgesia, first in the normal then the abnormal mother. This book is refreshingly different, although the first part begins traditionally enough with an account of maternal physiology followed by an outline of maternal and fetal morbidity, but it subsequently adheres to its title and is problem orientated. It is not, nor is it intended to be, an introductory text to obstetric anaesthesia.

Of the 577 pages, only 40, the second part, are concerned with anaesthesia and analgesia for the uncomplicated patient, the remainder relate to disorders of pregnancy and pregnancy in the presence of a comprehensive number of medical and surgical disorders. Maternal disease, either concomitant or pregnancy-induced are dealt with systematically; neurological, cardiac, respiratory, endocrine and haematological disorders are described in considerable detail. The fetus is well served and problems that relate to assessment of fetal welfare, fetal distress, premature delivery, and abnormal presentation are given valuable prominence. In the final section what are described as special problems are considered: pregnancy-induced hypertension, diabetes, the effects of extremes of age, trauma, *in vitro* fertilisation, substance abuse and nonobstetric surgery.

A succinct and valuable overview of the pathophysiological features and the known effects of pregnancy is given in the majority of chapters. Rare disorders, for example fungal pneumonia and acquired heart disease are given useful prominence. Little but anecdotal evidence is available in many instances, but the majority of the contributors acknowledge this and offer sensible and informed advice, based on the physiological principles outlined. This is a successful compilation, despite the predictably nonuniform style and repetitiveness inherent in the multi-author approach. There is a great deal of knowledge here that cannot be readily found in a single source. The chapter on the obese parturient is particularly valuable. What is presented is the best of American practice which differs significantly from that in the UK. However, litigation is a factor of increasing concern, as in the UK; clinical freedom is being eroded and obstetric care, we are informed, is now commonly shaped by what is called 'the prevailing standard of care', a chilling thought.

It is easy to be critical of books like this, since practices differ and do not necessarily reflect a reviewer's prejudices. However this book is recommended on its strengths: the enormous detail, the references and the sheer breadth of subjects covered. It is well produced with clear line drawings, and despite its length, concise. I enjoyed and welcome it as an excellent reference book.

J. Thorburn

## Manual of drug interactions for anesthesiology

R.A. Mueller and D.B.A. Lundberg. Pp. xlvii + 336. Churchill Livingstone, 1988. £19.95.

A pocket-sized paperback, for less than £20, that promises to detail all interactions that may occur between patient's current therapy and an anaesthetic regimen, sounds an attractive proposition. Add to that a brief description for each drug of its chief uses and side effects, and the pill becomes even sweeter.

The reality, sadly, is less impressive. There is a good opening chapter, labelled rather grandly 'Philosophy and Theory' (of Drug Interactions), which provides a clear resumé of the mechanisms which underly most drug interactions. The remainder of the book consists of a comprehensive listing of all medicines that a patient might be taking, with a brief description under each entry of the mechanism of action, uses, principal side effects, and possible anaesthetic implications.

Unfortunately, being a Swedish–American coproduction, a number of the drugs listed are of little relevance to British practice and other drugs are difficult to identify positively because of difference in nomenclature. The more than 600 drugs are not listed alphabetically, but grouped into sections related to their activity (cardiovascular, diuretics etc.), though no section headings are included. This makes use of the index mandatory to find any drug entry; this becomes irritating after a while.

The absence of any references, explained by the authors by the need to keep the book to a handy size, does lessen its usefulness. There is no way that the reader can verify entries which seem unfamiliar, nor is there any way of checking entries to assess the real significance of the advice proffered. Examination students will find the lack of sources doubly frustrating, although this is not the prime target group for this work.

This book, if available in the theatre suite, will certainly provide greater information of possible interactions than could be obtained from the British National Formulary. However, an edition using British nomenclature, with alphabetical listings and supporting references, would be considerably more useful.

P.F. TATHAM

**Books received**

We thank the publishers for the following books.

**Pulmonary vascular physiology and pathophysiology.**

Edited by E.K. WEIR AND J.T. REEVES. Pp. xvi + 762. Marcel Dekker, 1989. $125 USA and Canada; $150 all other countries.

**Orofacial pains—classification, diagnosis and management, 4th edn.**

W.E. BELL. xxii + 448. Year Book Medical, 1989. £44.50.

**Baillière's Clinical Anaesthesiology, vol. 2 No. 2. Some aspects of anaesthetic safety.**

Edited by O.P. DINNICK AND P.W. THOMPSON. Pp. x + 440 (page numbers continue from No. 1). Baillière Tindall, 1988. £15.00.

*Anaesthesia*, 1989, Volume 44, pages 623–626

# Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for March 1989. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences,* published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

## Abdominal surgery

Intercostal blockade and pulmonary function after cholecystectomy. Ross WB, Tweedie JH *et al. Surgery* 1989; **105:** 166.

Effects of epidural bupivacaine and epidural morphine on bowel function and pain after hysterectomy. Thoren T, Sundberg A *et al. Acta Anaesthesiologica Scandinavica* 1989; **33:** 181.

### *Adrenergic drugs and their antagonists*

Dopaminergic neurons—basic aspects. Bartholini G, Zivkovic B, Scatton B. In: Trendelenburg U, Weiner N, eds. *Catecholamines II.* Berlin: Springer-Verlag, 1989: 277.

Regulation of catecholamine development. Jonakait GM, Black IB. In: Trendelenburg U, Weiner N, eds. *Catecholamines II.* Berlin: Springer-Verlag, 1989: 13.

The effects of propranolol, phentolamine, and atropine on canine coronary vascular gradients. Klassen GA, Armour A, Garner JB. *Canadian Journal of Physiology and Pharmacology* 1989; **67:** 140.

Vascular effects of clonidine in patients with tetraplegia and unilateral brachial plexus injury. Kooner JS, Stone F *et al. Clinical and Experimental Hypertension* 1988; **10** (Suppl. 1): 405.

Propranolol antagonizes hypotension induced by alpha-blockers but not by sodium nitroprusside or methacholine. Tabrizchi R, Cheuk CYP. *Canadian Journal of Physiology and Pharmacology* 1989; **67:** 83.

Rate and extent of absorption of clonidine from a transdermal therapeutic system. Toon S, Hopkins K *et al. Journal of Pharmacy and Pharmacology* 1989; **41:** 17.

Basic pharmacology of alpha-adrenoceptor antagonists and hybrid drugs. Vanzwieten PA. *Journal of Hypertension* 1988; **6** (Suppl. 2): S3.

## Pharmacology

### *Anaesthetic agents*

Halothane-induced hepatic microsomal lipid peroxidation in guinea pigs and rats. Akita S, Kawahara M *et al. Journal of Applied Toxicology* 1989; **9:** 9.

Inhibition of platelet aggregation by some benzodiazepines. Cuparencu B, Trif I *et al. Current Therapeutic Research* 1989; **45:** 198.

Buspirone: a new nonbenzodiazepine anxiolytic agent. Funck-Brentano C. *American Journal of the Medical Sciences* 1989; **297:** 49.

Cimetidine and ranitidine do not affect enflurane metabolism in surgical patients. Oikkonen M, Rosenberg PH, Saarnivaara L. *Acta Anaesthesiologica Scandinavica* 1989; **33:** 129.

Blood gas tensions, acid-base status and CV function in miniature swine anaesthetized with halothane and methoxyflurane or IV metomidate hydrochloride. Svendsen P, Carter AM. *Pharmacology and Toxicology* 1989; **64:** 88.

### *Analgesic agents*

Cardiovascular effects of morphine during hypothermia. Alcaraz C, Bansinath M *et al. Archives Internationales de Pharmacodynamie et de Therapie* 1989; **297:** 133.

Antagonism of morphine analgesia by CCK-8-S does not extend to all assays for all opiate analgesics. Barbaz BS, Hall NR, Liebman JM. *Peptides* 1988; **9:** 1295.

Clinical pharmacokinetics of non-opiate abused drugs. Busto U, Bendayan R, Sellers EM. *Clinical Pharmacokinetics* 1989; **16:** 1.

Intracisternal naloxone and cardiac nerve blockade prevent vasodilatation during simulated haemorrhage in awake rabbits. Evans RG, Ludbrook J, Potocnik SJ. *Journal of Physiology* 1989; **409:** 1.

Fentanyl-induced ventilatory depression: effects of age. Hertzka RE, Gauntlett IS *et al. Anesthesiology* 1989; **70:** 213.

Stereospecific reversal of nitrous oxide analgesia by naloxone. Moody EJ, Mattson M *et al. Life Sciences* 1989; **44:** 703.

### *Muscle relaxants*

Anaphylaxis due to suxamethonium in a 7-year-old child: a 14-year follow-up with allergy testing. Assem ESK, Symons IE. *Anaesthesia* 1989; **44:** 121.

Gallamine exerts biphasic allosteric effects at muscarinic receptors. Ellis J, Seidenberg M. *Molecular Pharmacology* 1989; **35:** 173.

Effects of subacute administration of physostigmine on blood acetylcholinesterase activity, motor performance, and soman intoxication. Harris LW, Anderson DR *et al. Toxicology and Applied Pharmacology* 1989; **97:** 267.

Acetylcholinesterase prophylaxis against organophosphate poisoning. Quantitative correlation between protection and blood-enzyme level in mice. Raveh I, Ashani Y *et al. Biochemical Pharmacology* 1989; **38:** 529.

### *Other drugs*

The effects of lisuride, terguride and bromocriptine on intraocular pressure (IOP). Al-Sereiti MR, Turner P. *British Journal of Clinical Pharmacology* 1989; **27:** 159.

Editorial review: Mechanisms of aminoglycoside nephrotoxicity. Bennett WM. *Clinical and Experimental Pharmacology and Physiology* 1989; **16:** 1.

Clinical pharmacokinetics of clofazimine: a review. Holdiness MR. *Clinical Pharmacokinetics* 1989; **16:** 74.

Effect of Wy-45, 727 on 24 intragastric acidity in twenty normal volunteers. Merki HS, Kaufmann D *et al. British Journal of Clinical Pharmacology* 1989; **27:** 135.

## Apparatus

Principles of pulse oximetry: theoretical and practical considerations. Alexander CM, Teller LE, Gross JB. *Anesthesia and Analgesia* 1989; **68:** 368.

Evaluation of electrode polarity on defibrillation efficacy. Bardy GH, Ivey TD *et al. American Journal of Cardiology* 1989; **63:** 433.

Evaluation of the elastic behaviour of central venous PVC, polyurethane and silicone catheters. Cervera M, Dolz M *et al. Physics in Medicine and Biology* 1989; **34:** 177.

Automatic control of arterial pressure after cardiac surgery. Evaluation of microcomputer-based control using glyceryl trinitrate and sodium nitroprusside. Colvin JR, Kenny GNC. *Anaesthesia* 1989; **44:** 37.

---

The collator of this section is Dr L. Kaufman, MD, FFARCS, 145 Harley Street, London W1N 2DE. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Cannulation of inferior vena cava for long term central venous access. Curtas S, Bonaventura M, Meguid MM. *Surgery, Gynecology and Obstetrics* 1989; **168:** 121.

Early detection of inadvertent oesophageal intubation — pulse oximetry versus capnography. Guggenberger H, Lenz G, Federle R. *Acta Anaesthesiologica Scandinavica* 1989; **33:** 112.

Methods of measuring skin blood flow. Swain ID, Grant LJ. *Physics in Medicine and Biology* 1989; **34:** 151.

### Complications

Laryngospasm and reflex central apnoe caused by aspiration of refluxed gastric content in adults. Bortolotti M. *Gut* 1989; **30:** 233.

Biochemical basis for alcohol-induced liver injury. French SW. *Clinical Biochemistry* 1989; **22:** 41.

Psychogenic respiratory distress. Walker FO, Alessi AG *et al.* *Archives of Neurology* 1989; **46:** 196.

### General anaesthetic procedures

Metabolic responses ($V\text{o}_2$, $V\text{co}_2$ and energy expenditure) — associated with nasal intubation of the trachea. Fassoulaki A, Eforakopoulou M, Vassiliou M. *Anesthesia and Analgesia* 1989; **68:** 112.

Prevention of intraoperative hypothermia. Kristensen G, Guldager H, Gravesen H. In: Lomax P, Schonbaum E, eds. *Thermoregulation: research and clinical applications.* Basel: S. Karger; 1989: 16.

Postoperative tremor. Sessler DI, Israel DS *et al.* In: Lomax P, Schonbaum E, eds. *Thermoregulation: research and clinical applications.* Basel: S. Karger, 1989: 18.

Perianesthetic thermoregulation. Sessler DI, Olofsson CI, Rubinstein E. In: Lomax P, Schonbaum E, eds. *Thermoregulation: research and clinical applications* Basel: S. Karger, 1989: 11.

### General interest

Specificity spillover at the hormone receptor — exploring its role in human disease. Fradkin JE, Eastman RC *et al.* *New England Journal of Medicine* 1989; **320:** 640.

Systemic blood pressure and intraocular pressure relationship. Gherezghiher T, Hey JA, Koss MC. *Journal of Ocular Pharmacology* 1988; **4:** 291.

Current concepts — Geriatrics: delirium in the elderly patient. Lipowski ZJ. *New England Journal of Medicine* 1989; **320:** 578.

The oculocardiac reflex in blepharoplasty surgery. Matarasso A. *Plastic and Reconstructive Surgery* 1989; **83:** 243.

### Local analgesia

The comparative effects of bupivacaine epidural analgesia on postoperative rewarming. Bernard JM, Hommeril JL *et al.* In: Lomax P, Schonbaum E, eds. *Thermoregulation: research and clinical applications.* Basel: S. Karger, 1989: 24.

Cardiotoxicity of ropivacaine — a new amide local anaesthetic agent. Reiz S, Haggmark S *et al.* *Acta Anaesthesiologica Scandinavica* 1989; **33:** 93.

### Spinal and epidural analgesia

The lumbar epidural space in patients examined with epiduroscopy. Blomberg RG, Olsson SS. *Anesthesia and Analgesia* 1989; **68:** 157.

Effect of epidural lidocaine on spinal cord blood flow. Mitchell P, Goad CW *et al.* *Anesthesia and Analgesia* 1989; **68:** 312.

### Spinal opioids

Intrathecal fentanyl depresses nociceptive flexion reflexes in patients with chronic pain. Chabal C, Jacobson L, Little J. *Anesthesiology* 1989; **70:** 226.

Spinal analgesia with morphine and clonidine. Kitahata LM. *Anesthesia and Analgesia* 1989; **68:** 191.

Epidural morphine delays gastric emptying and small intestinal transit in volunteers. Thoren T, Tanghoj H *et al.* *Acta Anaesthesiologica Scandinavica* 1989; **33:** 174.

### Obstetric anaesthesia and analgesia

Pulmonary and ventilatory responses to pregnancy, immersion, and exercise. Berry MJ, McMurray RG, Katz VL. *Journal of Applied Physiology* 1989; **66:** 857

Thyrotoxicosis complicating pregnancy. Davis LE, Lucas MJ *et al.* *American Journal of Obstetrics and Gynecology* 1989; **160:** 63.

Measurement of cardiac output in pregnancy by thermodilution and impedance techniques. Easterling TR, Benedetti TJ *et al.* *British Journal of Obstetrics and Gynaecology* 1989; **96:** 1.

Use of anticoagulants during pregnancy. Ginsberg JS, Hirsh J. *Chest* 1989; **92** (No. 2) (Suppl.): S156.

Evidence for functional thromboxane A2-prostaglandin H2 receptors in human placenta. Hedberg A, Mento PF *et al.* *American Journal of Physiology* 1989; **256** (No. 2 Part 1): E256.

Recurrent diabetes insipidus associated with pregnancy — pathophysiology and therapy. Hughes JM, Barron WM, Vance ML. *Obstetrics and Gynecology* 1989; **73:** 462.

Acute intermittent porphyria in pregnancy. Milo R, Newman M *et al.* *Obstetrics and Gynecology* 1989; **73:** 450.

Physiologic role of endogenous human atrial natriuretic peptide in preeclamptic pregnancies. Miyamoto S, Shimokawa H *et al.* *American Journal of Obstetrics and Gynecology* 1989; **160:** 155.

Intrapartum fetal heart rate patterns in pregnancies complicated by hypertension — A cohort study. Montan S, Ingemarsson I. *American Journal of Obstetrics and Gynecology* 1989; **160:** 283.

Anesthesia for cesarean section—effects on neonates. Ong BY, Cohen MM, Palahniuk RJ. *Anesthesia and Analgesia* 1989; **68:** 270.

Influence of ritodrine on plasma steroids and human placental lactogen levels in third-trimester pregnancies. Schreyer P, Zer Y *et al.* *Gynecologic and Obstetric Investigation* 1989; **27:** 10.

Aldosterone is secreted intermittently during pregnancy. Stevens KJ, Paintin DB, Few JD. *British Journal of Obstetrics and Gynaecology* 1989; **96:** 80.

### Paediatric anaesthesia and intensive care

High-frequency jet ventilation in neonatal pulmonary hypertension. Carlo WA, Chatbum RL *et al.* *American Journal of Diseases of Children* 1989; **143:** 233.

Hemorrhagic shock and encephalopathy—reflections about a new devastating disorder that affects normal children. Chesney PJ, Chesney RW. *Journal of Pediatrics* 1989; **114:** 254.

Hypoxic–ischemic spinal cord injury following perinatal asphyxia. Clancy RR, Sladky JT, Rorke LB. *Annals of Neurology* 1989; **25:** 185.

Mortality with increasing assisted ventilation of very-low-birth-weight infants. Doyle LW, Murton LJ, Kitchen WH. *American Journal of Diseases of Children* 1989; **143:** 223.

Paediatric drug dosing: body-weight versus surface area. Maxwell GM. *Drugs* 1989; **37:** 113.

Placental barrier to atrial natriuretic peptide in rats. Mulay S, Varma DR. *Canadian Journal of Physiology and Pharmacology* 1989; **67:** 1.

Comparison of airway pathologic lesions after high-frequency jet or conventional ventilation. Polak MJ, Donnelly WH, Bucciarelli RL. *American Journal of Diseases of Children* 1989; **143:** 228.

Circuit diagram of the circulation of cerebrospinal fluid. Rekate HL In: Marlin AE, ed. *Concepts in pediatric neurosurgery, Vol. 9.* Basel: S. Karger, 1989: 46.

Intraventricular hemorrhage in the premature infant—current concepts. Part II. Volpe JJ. *Annals of Neurology* 1989; **25:** 109.

Hypoxia reinforces laryngeal reflex bradycardia in infants. Wennergren G, Hertzberg T *et al.* *Acta Paediatrica Scandinavica* 1989; **78:** 11.

Pharmacokinetics of ranitine in critically ill infants. Wiest DB, O'Neal W *et al.* *Developmental Pharmacology and Therapeutics* 1989; **12:** 7.

Pediatric regional anesthesia. Yaster M, Maxwell LG. *Anesthesiology* 1989; **70:** 324.

### Cardiovascular system

*Physiology*

Differences in coagulation and fibrinolysis after traumatic and septic shock in man. Bagge L, Haglund O *et al.* *Scandinavian Journal of Clinical and Laboratory Investigation* 1989; **49:** 63.

Clinical aspects of disseminated intravascular coagulation: a clinican's point of view. Baker WF jr. *Seminars in Thrombosis and Hemostasis* 1989; **15:** 1.

Evidence for two functionally distinct vasomotor subregions of rostral ventral medulla. Cox BF, Brody MJ. *Clinical and Experimental Hypertension* 1988; **10** (Suppl. 1): 11.

Hemostasis and fibrinolysis in renal transplantation. Faulk WP, Gargiulo P *et al. Seminars in Thrombosis and Hemostasis* 1989; **15:** 88.

Studies on the origin and generation of sympathetic nerve activity. Gebber GL, Barman SM. *Clinical and Experimental Hypertension* 1988; **10** (Suppl. 1): 33.

Enhanced hypoxic pulmonary vasoconstriction in hypertension. Guazzi MD, Alimento M *et al. Circulation* 1989; **79:** 337.

Prehormone atrial natriuretic peptides increase in proportion to right ventricular pacing rate. Lam N, Wyeth RP *et al. American Heart Journal* 1989; **117:** 385.

Natriuresis associated with elevated plasma atrial natriuretic hormone during supraventricular tachycardia. Nicklas JM, Giacherio DA *et al. American Heart Journal* 1989; **117:** 377.

Human hemopoietic growth factors. Platter E. *European Journal of Haematology* 1989; **42:** 1.

The anti-arrhythmic effects of myocardial ischaemia—relation to reperfusion arrhythmias. Podzuweit T, Binz K H *et al. Cardiovascular Research* 1989; **23:** 81.

Diagnostic value of longterm ambulatory ECG in patients with syncope, dizziness or palpitations. Ringqvist I, Jonason T *et al. Clinical Physiology* 1989; **9:** 47.

Vasoconstrictor mechanisms in congestive heart failure. 1. Zelis R, Sinoway L *et al. Modern Concepts of Cardiovascular Disease* 1989; **58:** 7.

Vasoconstrictor mechanisms in congestive heart failure. 2. Zelis R, Sinoway L *et al. Modern Concepts of Cardiovascular Disease* 1989; **58:** 13.

### *Treatment and medication*

Comparison of enalapril versus digoxin for congestive heart failure. Beaune J. *American Journal of Cardiology* 1989; **63** (No. 8): D22.

Anaesthetic management of the patient with a permanent pacemaker. Bloomfield P, Bowler GMR. *Anaesthesia* 1989; **44:** 42.

What we would like to know about antihypertensive mechanisms of angiotensin converting enzyme inhibition. Brunner HR, Waeber B, Nussberger J. *Journal of Hypertension* 1988; **6:** S1.

Use of the automatic external defibrillator in homes of survivors of out-of-hospital ventricular fibrillation. Eisenberg MS, Moore J *et al. American Journal of Cardiology* 1989; **63:** 443.

Misuse of verapamil in pre-excited atrial fibrillation. Garratt C, Antoniou A *et al. Lancet* 1989; **1:** 367.

Medicolegal considerations in the initiation and termination of resuscitation in Canada. Gilmour JM, Rosenberg PJ. *Canadian Medical Association Journal* 1989; **140:** 279.

Early use of metoprolol and serum potassium in suspected acute myocardial infarction. Herlitz J, Hjalmarson A, Waagstein F. *International Journal of Cardiology* 1989; **22:** 169.

Chronic stable angina monotherapy—nifedipine versus propanolol. Higginbotham MB, Morris KG *et al. American Journal of Medicine* 1989; **86** (1A): 1.

Enalapril for congestive heart failure. Kjekshus J, Swedberg K. *American Journal of Cardiology* 1989; **63** (No. 8): D26.

How to digitalize and to maintain optimal digoxin levels in congestive heart failure. Lambert C, Rouleau JL. *Cardiovascular Drugs and Therapy* 1989; **2:** 717.

The effect of transfusion of fresh whole blood versus platelet concentrates after cardiac operations. Lawee J, Martinowitz U *et al. Journal of Thoracic and Cardiovascular Surgery* 1989; **97:** 204.

Surgical treatment of hypertrophic obstructive cardiomyopathy. Leading Article *Lancet* 1989; **1:** 358.

Reduction of ventricular arrhythmias by atropine during coronary arteriography. Lehmann KG, Chen YCJ. *American Journal of Cardiology* 1989; **63:** 447.

Thrombolysis in the management of acute myocardial infarction and unstable angina pectoris. Loscalzo J. *Drugs* 1989; **37:** 191.

Current management of venous thromboembolic disease. McCann RL, Sabiston DC. *British Journal of Surgery* 1989; **76:** 113.

Clinical pharmacokinetics and therapeutic use of hydralazine in congestive heart failure. Mulrow JP, Crawford MH. *Clinical Pharmacokinetics* 1989; **16:** 86.

Taurine: effect on myocardial relaxation. Rahimi AR, Campbell KB *et al. Clinical and Experimental Pharmacology and Physiology* 1989; **16:** 41.

Efficacy of urapidil in the management of essential hypertension—a comparison with captopril. Rosenthal J, Haerlin R. *Journal of Hypertension* 1988; **6** (Suppl. 2): S69.

Cardiac and vascular effects of atrial natriuretic factor and sodium nitroprusside in healthy men. Roy LF, Oglivie RI *et al. Circulation* 1989; **79:** 383.

Heparin anticoagulation. Scheinberg P. *Stroke* 1989; **20:** 173.

Management of myocardial infarction shock: current status. Schreiber TL, Miller DH *et al. American Heart Journal* 1989; **117:** 435.

Randomized trial of primary anesthetic agents on outcome of coronary artery bypass operations. Slogoff S, Keats AS. *Anesthesiology* 1989; **70:** 179.

Enhancement of angiotensin-converting enzyme activity in the inner cortex of rat kidney by captopril. Song GB, Tominaga M *et al. Renal Physiology and Biochemistry* 1988; **11:** 43.

Efficacy of medical therapy tailored for severe congestive heart failure in patients transferred for urgent cardiac transplantation. Stevenson LW, Dracup KA, Tillisch JH. *American Journal of Cardiology* 1989; **63:** 461.

The effects of amiloride on biliary calcium and cholesterol gallstone formation. Strichartz SD, Abedin MZ *et al. Annals of Surgery* 1989; **209:** 152.

Complications of plasma exchange. Sutton DMC, Nair RC *et al. Transfusion* 1989; **29:** 124.

Enalapril: an update of its pharmacological properties, and therapeutic use in congestive heart failure. Todd PA, Goa KL. *Drugs* 1989; **37:** 141.

Does choice of anesthetic agent significantly affect outcome after coronary artery surgery? Tuman KJ, McCarthy RJ *et al. Anesthesiology* 1989; **70:** 189.

Long-term oral therapy of congestive heart failure with phosphodiesterase inhibitors. Wood MA, Hess ML. *American Journal of the Medical Sciences* 1989; **297:** 105.

## Respiration

### *Physiology*

Metabolic and functional adaptation of the diaphragm to training with resistive loads. Akabas SR, Bazzy AR *et al. Journal of Applied Physiology* 1989; **66:** 529.

Preferential axial flow during high-frequency oscillations: effects of gas density. Alleyne CM, Frantz ID III, Fredberg J. *Journal of Applied Physiology* 1989; **66:** 542.

Hyperoxia and moderate hypoxia fail to affect inspiratory muscle fatigue in humans. Ameredes BT, Clanton TL. *Journal of Applied Physiology* 1989; **66:** 894.

Postoperative mixed venous oxygen saturation monitoring. Baron JF, Bensouda A, Coriat P. *Applied Cardiopulmonary Pathophysiology* 1988; **2:** 327.

Recovery of diaphragm function after laparotomy and chronic sonomicrometer implantation. Easton PA, Fitting JW *et al. Journal of Applied Physiology* 1989; **66:** 613.

Oxygen free radicals mediate ischemia-induced lung injury. Klausner JM, Patterson IS *et al. Surgery* 1989; **105:** 192.

Determination of the oxygen cost of level walking. Linnarsson D, Mattsson E *et al. Clinical Physiology* 1989; **9:** 1.

Reflex effect of esophageal distension on respiratory muscle activity and pressure. Oliven A, Hazhiu M, Kelsen SG. *Journal of Applied Physiology* 1989; **66:** 536.

Mixed venous oxygen saturation. Reinhart K, Schafer M *et al. Applied Cardiopulmonary Pathophysiology* 1988; **2:** 315.

### *Treatment and medication*

Nocturnal oxygen therapy does not improve snorer's intelligence. Block AJ, Hellard DW, Switzer DA. *Chest* 1989; **95:** 274.

Double-lung transplant for advanced chronic obstructive lung disease. Cooper JD, Patterson GA *et al. American Review of Respiratory Disease* 1989; **139:** 301.

Cardiopulmonary effects of high frequency positive-pressure ventilation versus jet ventilation in respiratory failure. Courtney SE, Spohn WA *et al. American Review of Respiratory Disease* 1989; **139:** 504.

Continuous monitoring of mixed venous oxygen saturation as an indicator of pharmacologic intervention. Hassan E, Green JA *et al. Chest* 1989; **95:** 406.

Preoperative spirometry before abdominal operations—a critical appraisal of its predictive value. Lawrence VA, Page CP, Harris GD. *Archives of Internal Medicine* 1989; **149:** 280.

Respiratory management after cardiac surgery. Matthay MA, Wienerkronish JP. *Chest* 1989; **95:** 89.

Determinants of weaning and survival among patients with COPD who require mechanical ventilation for acute respiratory failure. Menzies R, Gibbons W, Goldberg P. *Chest* 1989; **95:** 398.

Acute management of laryngeal trauma. Update. Schaefer SD, Close LG. *Annals of Otology, Rhinology and Laryngology* 1989; **98:** 98.

A comparison between the airway response to isocapnic hyperventilation and hypertonic saline in subjects with asthma. Smith CM, Anderson SD. *European Respiratory Journal* 1989; **2:** 36.

Conventional versus high frequency jet ventilation with a bronchopleural fistula. Spinale FG, Linker RW *et al. Journal of Surgical Research* 1989; **46:** 147.

Portable oxygen therapy: use and benefit in hypoxaemic COPD Patients on long-term oxygen therapy. Vergeret J, Brambilla C, Mounier L. *European Respiratory Journal* 1989; **2:** 20.

Control of larynx in patients with obstructive and restrictive pulmonary impairment. Yanai M, Sekizawa K *et al. European Respiratory Journal* 1989; **2:** 31.

## Central nervous system

### *Physiology*

Effect of activation of central nervous system serotonin 1A receptors on cardiorespiratory function. Gillis RA, Hill KJ *et al. Journal of Pharmacology and Experimental Therapeutics* 1989; **248:** 851.

Changes in cranial CSF volume during hypercapnia and hypocapnia. Grant R, Condon B *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1989; **52:** 218.

Endogenous opioid systems and the regulation of dendritic growth and spine formation. Hauser KF, McLaughlin PJ, Zagon IS. *Journal of Comparative Neurology* 1989; **281:** 13.

Changes of blood flow in the cerebral cortex after subcortical ischemic infarction. Hojerpedersen E, Petersen OF. *Stroke* 1989; **20:** 211.

Intracranial pressure and obstructive sleep apnea. Jennum P, Borgesen SE. *Chest* 1989; **95:** 279.

Cerebral blood flow and cerebral oxygen consumption during nitroprusside-induced hypotension to less than 50 mmHg. Pinaud M, Souron R *et al. Anesthesiology* 1989; **70:** 255.

Cerebral blood flow does not change following sodium nitroprusside infusion during hypothermic cardiopulmonary bypass. Rogers AT, Prough DS *et al. Anesthesia and Analgesia* 1989; **68:** 122.

Sympathetic activation by hypoxia and hypercapnia—implications for sleep apnea. Somers VK, Mark AL, Abboud FM. *Clinical and Experimental Hypertension* 1988; **10** (Suppl. 1)**:** 413.

### *Treatment and medication*

Spinal cord ischemia—an evaluation of pharmacologic agents in minimizing paraplegia after aortic occlusion. Kirshner DL, Kirshner RL *et al. Journal of Vascular Surgery* 1989; **9:** 305.

Clinical pharmacology of antipsychotic drugs. Lader M. *Journal of International Medical Research* 1989; **17:** 1.

A comparative trial of a new antidepressant, fluoxetine. Levine S, Deo R, Mahadevan K. *International Clinical Psychopharmacology* 1989; **4** (Suppl. 1)**:** 41.

The risk of ischaemic brain damage during the use of self-retaining brain retractors. Rosenorn J. *Acta Neurologica Scandinavica* 1989; **79** (Suppl. 120)**:** 9.

Triazolam: adverse effects in relation to dosage. Schou SJ. *Pharmacology and Toxicology* 1989; **64:** 6.

Parkinson's disease. Wolters EC, Calne DB. *Canadian Medical Association Journal* 1989; **140:** 507.

## Endocrine and metabolic

### *Physiology*

Vasopressin micro-injections into the nucleus tractus solitarii decrease heart rate and blood pressure in anaesthetized rats. Brattstrom A, Dejong W, Dewied D. *Journal of Hypertension* 1988; **6** (Suppl. 4)**:** S521.

Vasopressin and ANG II in the control of ACTH secretion and arterial and atrial pressures. Brooks VL. *American Journal of Physiology* 1989; **256** (no. 2 Part 2)**:** R339.

The pathophysiology of lactic acidosis. Cohen RD. *Applied Cardiopulmonary Pathophysiology* 1988; **2:** 285.

Effects of mannose and fructose on the synthesis and secretion of Insulin. Curry DL. *Pancreas* 1989; **4:** 2.

Renal microvascular effects of vasopressin and vasopressin antagonists. Edwards RM, Trizna W, Kinter LB. *American Journal of Physiology* 1989; **256** (No. 2 Part 2)**:** F274.

Plasma histamine concentrations are elevated in patients with diabetes mellitus and peripheral vascular disease. Gill DS, Barradas MA *et al. Metabolism* 1989; **38:** 243.

Events leading to insulin-dependent diabetes. Leslie RDG, Lazarus NR, Vergani D. *Clinical Science* 1989; **76:** 119.

Immunoreactive oxytocin and vasopressin in the non-pregnant human uterus and oviductal isthmus. Lundin S, Forman A *et al. Acta Endocrinologica* 1989; **120:** 239.

Baroreceptor influences on oxytocin and vasopressin secretion. Morris M, Alexander N. *Hypertension* 1989; **13:** 110.

Clearance and urinary excretion of vasopressin in conscious dogs. Sondeen JL, Claybaugh JR. *American Journal of Physiology* 1989; **256** (No. 2 Part 2)**:** R291.

Insulin deficiency in non-insulin-dependent diabetes. Temple RC, Carrington CA *et al. Lancet* 1989; **1:** 293.

Saturable pharmacokinetics in the renal excretion of drugs. Van Ginneken CAM, Russel FGM. *Clinical Pharmacokinetics* 1989; **16:** 38.

Renal failure complicating obstructive jaundice. Wait RB, Kahng KU. *American Journal of Surgery* 1989; **157:** 256.

Pseudohyponatremia—a reappraisal. Weisberg LS. *American Journal of Medicine* 1989; **86:** 315.

### *Treatment and medication*

Effects of the opiate agonist loperamide on pituitary–adrenal function in patients with suspected hypercotisolism. Ambrosi B, Bochicchio D *et al. Journal of Endocrinological Investigation* 1989; **12:** 31.

Central control of anterior pituitary function. Arnold MA, Martin JB. In: Trendelenburg U, Weiner N eds. *Catecholamines II*. Berlin: Springer-Verlag, 1989: 89.

Glucose control and the renal and retinal complications of insulin-dependent diabetes. Chase HP, Jackson WE *et al. Journal of the American Medical Association* 1989; **261:** 1155.

Effect of nutritional status on acute phase protein response to elective surgery. Cruickshank AM, Hansell DT *et al. British Journal of Surgery* 1989; **76:** 165.

Alpha-adrenoceptors and the kidney. Deleeuw PW, Birkenhager WH. *Journal of Hypertension* 1988; **6** (Suppl. 2)**:** S21.

Response by the neurotensin systems of the basal ganglia to cocaine treatment. Hanson GR, Smiley P *et al. European Journal of Pharmacology* 1989; **160:** 23.

Pharmacokinetic–pharmacodynamic relationships of oral hypoglycaemic agent: an update. Marchetti P, Navalesi R. *Clinical Pharmacokinetics* 1989; **16:** 100.

Bromocriptine and pleuropulmonary disease. Melmed S, Braunstein GD. *Archives of Internal Medicine* 1989; **149:** 259.

Pharmacologic modulation of experimental postischemic hepatic function. Ontell SJ, Makowka L *et al. Annals of Surgery* 1989; **209:** 200.

A randomized trial of intensive insulin therapy in newly diagnosed insulin-dependent diabetes mellitus. Shah SC, Malone JI, Simpson NE. *New England Journal of Medicine* 1989; **320:** 550.

Protein binding characteristics of bumetanide. Walker PC, Berry NS, Edwards DJ. *Developmental Pharmacology and Therapeutics* 1989; **12:** 13.

## Pain

### *Treatment and medication*

The influence of patient characteristics on the requirements for postoperative analgesia. A reassessment using patient-controlled analgesia. Burns JW, Hodsman NBA *et al. Anaesthesia* 1989; **44:** 2.

Pharmacy-initiated introduction of patient-controlled analgesia to a 400-bed community hospital. McKenna TR, Branigan TA, Sorocki AH. *American Journal of Hospital Pharmacy* 1989; **46:** 291.

*Anaesthesia*, 1989, Volume 44, pages 627–629

# Obituaries

**Armstrong,** David Mouat, OBE, FFARCS, formerly Consultant Anaesthetist to Ayrshire Hospitals. Qualified from University of Glasgow in 1937.

**Clark,** Douglas Crawford, MB, BS, FFARCS, formerly Consultant Anaesthetist at Luton and Dunstable Hospital, and Honorary Assistant Anaesthetist at the Dental Department, University College Hospital, London. Qualified from London University in 1918.

**Dinsdale,** Tom, MB, ChB, FFARCS, formerly Consultant Anaesthetist at Manchester and Salford Area Health Authorities. Qualified from University of Manchester in 1937.

**Foulds,** Stanley Bond, MB, ChB, FFARCS, Consultant Anaesthetist at Salford Health Authority. Qualified from University of Manchester in 1956.

**Grimshaw,** Vernon Anthony, MB, BChir, FFARCS, formerly Consultant Anaesthetist at United Leeds Hospital. Qualified from University of Cambridge in 1951.

**Lithman,** Leslie Henry, MRCS, LRCP, FFARCS, formerly Consultant Anaesthetist at St Nicholas Hospital, Plumstead. Qualified from University of London in 1939.

**Parry,** John Wynne Lloyd, TD, BM, BCh, FFARCS, Consultant Anaesthetist at Aberdeen General Hospital. Qualified from Oxford and University College Hospital in 1955.

**Toner,** John Stannard, MB, BS, MRCS, LRCP, FFARCS. Qualified from The London Hospital in 1955.

**Wheldon,** John Tulloh, MB, BS, FFARCS. Consultant Anaesthetist at United Newcastle Hospital and Gateshead Group of Hospitals. Qualified from Durham University in 1944.

# International congress calendar

### 1989

**13–15 July.** London. *Refresher Course and Scientific Meeting of European Academy of Anaesthesiologists.*
*Information:* The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

**12–16 August.** Christchurch. *Combined Meeting of New Zealand Society with the Australian Society of Anaesthetists.*
*Information:* Secretariat, ASA NZ Society of Anaesthetists, P.O. Box 600, Edgecliffe, NSW 2027, Australia.

**15–18 August.** Washington DC, USA. *International Conference on Emergency Health Care Development.*
*Information:* Conference Organizers, MCDI, 1742 R Street N.W., Washington DC 2009, USA.

**23–25 August.** Oulu, Finland. *Scandinavian Meeting of the European Society of Regional Anaesthesia.*
*Information:* Secretariat, Scandinavian ESRA, Department of Anaesthesia, University of Oulu, SF 90220 Oulu, Finland.

**30 August–2 September.** Bonn, West Germany. *11th Annual Meeting of European Academy.*
*Information:* Professor Dr H. Stoeckel, Institut für Anaesthesiologie der Rheinischen Friedrich-Wilhelm-Universität, Sigmund Freud Str. 25, D 5300, Bonn 1, West Germany.

**31 August–2 September.** London. *IFAC Workshop on Decision Support for Patient Management: Measurement, Modelling and Control.*
*Information:* IFAC-BME 89, Bell Howe Conferences, Gothic House, Barker Gate, Nottingham, NG1 1JU.

**1–4 September.** Tunisia. *3rd Pan Arab Congress of Anaesthesia and Intensive Care.*
*Information:* Dr Jamal Al-Shanableh, P.O. Box 15404, Marka-Amman, Jordan.

**3–8 September.** Kyoto, Japan. *Fifth World Congress on Intensive and Critical Care Medicine.*
*Information:* The Fifth World Congress on Intensive and Critical Care Medicine, c/o Japan Convention Services Inc., Nippon Press Center Building 2-2-1 Uchisaiwai-cho, Chyoda-ku, Tokyo 100, Japan.

**7–9 September.** Tanzania. *Annual Scientific Conference of the Society of Anaesthesiologists of East Africa.*
*Information:* Dr H. Lweno, P.O. Box 7097, Dar es Salaam, Tanzania.

**10–14 September.** Freiburg. *8th Congress of European Society of Pneumology.*
*Information:* Professor Dr med. H. Matthys, Arztlicher Direktor, Abteilung Pneumologie, Robert-Koch-Klinik, Universität, D 7800 Freiburg, West Germany.

**10–15 September.** Hong Kong. *6th World Congress on Emergency and Disaster Medicine.*
*Information:* Dr M. Moles, c/o Meeting Planners, 701 Tung Wai Comm Bldg, 109 Gloucester Road, Wanchai, Hong Kong.

**12–15 September.** Surfers Paradise, Australia. *Post World Congress Meeting and 14th Australian and New Zealand Meeting on Intensive Care.*
*Information:* Dr R. Parkes, ICU of Prince Charles Hospital, Rode Road, Chermside, Queensland 4032, Australia.

**12–16 September.** Austria. *International Conference on Anaesthesia, Intensive Care and Emergency Medicine.*
*Information:* Professor Dr J.M. Hackl, University Klinik für Anaesthesia und Allg. Intensivemedizin, Anichstr. 35, A-6020, Innsbruck, Austria.

**13–15 September.** Swansea. *Linkman Conference and Annual Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
*Information:* Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

**14–15 September.** Osaka, Japan. *4th International Symposium of Endocrinology in Anaesthesia and Surgery.*
*Information:* Department of Anesthesiology, University of Hirosaki, School of Medicine, 5 Zaifu-cho, Hirosaki, Aomoriken, 036 Japan.

**16–19 September.** Herzliya, Israel. *The Second International Symposium–Pain 1989.*
*Information:* Pain 1989 Secretariat, POB 50006, Tel Aviv 61500, Israel.

**17–19 September.** Beijing. *1st International Symposium on Emergency Medicine.*
*Information:* Dr M. Moles, c/o Meeting Planners, 701 Tung Wai Comm Bldg., 109 Gloucester Road, Wanchai, Hong Kong.

**18–22 September.** London. *9th Congress of the Federation Internationale de Medecine Manuelle.*
*Information:* Conference Associates FIMM, 27A Medway Street, London, SW1P 2BD.

**19–22 September.** Tel Aviv. *15th International Congress of the Israel Society of Anesthesiologists.*
*Information:* Anesthesiologists 1989, P.O. Box 50006, Tel Aviv 61500, Israel.

**22–26 September.** Buenos Aires, Argentina. *XX Latin American Congress of Anaesthesiology.*
*Information:* Federacion Argentina de Asociaciones de

Anestesiologia, Aranguren 1323/27 (1405) Buenos Aires, Argentina.

**27–30 September.** Warsaw. *Joint Meeting between Association of Paediatric Anaesthetists of Great Britain and Ireland and Polish Society.*
*Information:* Dr J. Kacki, ul Kasprzaka 17A, 01-211 Warsaw, Poland.

**4–6 October.** Rome, Italy. *International Symposium on Survival under Critical Life Conditions.*
*Information:* Organizing Secretariat, Fondazione Giovanni Lorenzini, Via Monte Napoleone 23, 20121 Milan, Italy.

**4–7 October.** Tunis. *Third Pan Arab Congress on Anaesthesia and Intensive Care.*
*Information:* Secretary, P.O. Box 15404, Marka, Amman, Jordan.

**14–18 October.** New Orleans. *American Society of Anesthesiologists Annual Meeting.*
*Information:* Executive Secretary, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

**18–20 October.** Barcelona. *11th Congress of Chronical Roncopathy.*
*Information:* BRP, Edificio Layetana C-Pau Claris, 138, 08009, Barcelona, Spain.

**21 October.** London. *Postgraduate Study Day, Royal College of Surgeons of England, London, organised jointly with the College of Anaesthetists.*
*Information:* The Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

**26–28 October.** Berlin. *3rd International Steglitz Symposium on Clinical Aspects of $O_2$ Transport and Tissue Oxygenation.*
*Information:* M. Specht, Klinik für Anaesthesiologie und Operative Intensivmedizin, Klinikum Steglitz FU-Berlin, Hindenburgdamm 30, D-1000 Berlin 45.

**18–22 October.** Tokyo and Kyoto. *6th World Congress for Bronchology.*
*Information:* Dr M. Niitsuma, Secretary General, 6th World Congress for Bronchology, Department of Surgery, Tokyo Medical College, 6-7-1 Mishishinjuku, Shinjuku-ku, Tokyo 160 Japan.

**3–5 November.** Toronto, Canada. *Paediatric Anaesthesia Conference.*
*Information:* Paediatric Anaesthesia Conference, The Hospital for Sick Children, 555 University Avenue, Toronto, Ont. M5G 1X8, Canada.

**5–10 November.** Sao Paulo. *36th Brazilian Congress of Anesthesiology.*
*Information:* Congress Secretariat, Dr R.S. Mathias, Rua Caiubi 666, Sao Paulo, Brazil 05010.

**11–17 November.** River Rhine. *International Symposium to commemorate '60 years of surfactant research'.*
*Information:* Professor B. Lachmann, Department of Anesthesiology, Erasmus University, POB 1738, 3000 DR Rotterdam, The Netherlands.

**28 November–1 December.** Manila. *6th ASEAN Congress of Anaesthesiologists.*
*Information:* P.O. Box 4486, Manila, Philippines.

## 1990

**13–20 January.** Virgin Islands. *8th Annual Symposium on Clinical Update in Anesthesiology.*
*Information:* Dr G. Silvay, Dept. of Anesthesiology, Box 1010, Mount Sinai School of Medicine, 1 Gustave L. Levy Place, New York, NY 10029-6574.

**24–26 February.** New Orleans. *Mardi Gras Anaesthetic Course.*
*Information:* Alan Grogono, Tulane University Medical Centre, 1430 Tulane Avenue, New Orleans, Louisiana 70112, USA.

**10–14 March.** Honolulu. *64th Congress of the International Anaesthesia Research Society.*
*Information:* Emerson A. Moffitt, IARS, 3645 Warrensville Center Road, Cleveland, Ohio 44122, USA.

**17–23 March.** Durban, South Africa. *National Anaesthetic Congress.*
*Information:* Professor D.A. Rocke, 1990 Anaesthetic Congress, Department of Anaesthetics, P.O. Box 17039, Congella 4013, South Africa.

**27–30 March.** Brussels, *10th International Symposium on Intensive Care and Emergency Medicine.*
*Information:* Dr J.L. Vincent, Dept. of Intensive Care, Erasme University Hospital, Route de Lennik 808, 1070 Brussels, Belgium.

**4–6 April.** Glasgow. *Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
*Information:* Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

**13–19 May.** Wellington, New Zealand. *Faculty of Anaesthetics and the Royal Australasian College of Surgeons Annual General Meeting.*
*Information:* Administrative Officer, Faculty of Anaesthetists, RACS, Spring Street, Melbourne, Victoria 3000.

**5–8 June.** Amsterdam. *5th European Congress on Intensive Care Medicine 1990.*
*Information:* Secretariat, c/o Holland Organizing Centre, Lange Voorhout 16, 2514 EE, The Hague, The Netherlands.

**15–19 June.** Vancouver. *47th Annual Meeting of the Canadian Anaesthetists' Society.*
*Information:* Ms Ann Andrews, CAS 187, Gerrard St. E, Toronto, Ontario M5A 2E5 Canada.

**5–8 September.** Budapest, Hungary. *3rd International Symposium on Anesthesia for Cardiac Patients.*
*Information:* Dr G. Silvay, Department of Anesthesiology, Box 1010, Mount Sinai School of Medicine, 1 Gustave L. Levy Place, New York, NY 10029-6574, USA.

**9–15 September.** Warsaw. *VIIIth European Congress of Anaesthesiologie.*
*Information:* The Organising Committee, VIIIth European Congress of Anaesthesiology, c/o The Polish Society of Anaesthesiology and Intensive Therapy, ul. Kasprzaka 17a, 01-211 Warsaw, Poland.

**23–28 September.** Seoul. *8th Asian/Australasian Congress of Anaesthesia.*
*Information:* Department of Anesthesiology, Seoul National University Hospital, 28 Yungun-Doug, Chongro-Ku, Seoul 110.

**26–28 September.** Manchester. *Linkman Conference and Annual Scientific Meeting Exhibition.*
*Information:* The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

**19–23 October.** Las Vegas. *American Society of Anesthesiologists Annual Meeting.*
*Information:* Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

**5–10 November.** Sao Paulo. *36th Brazilian Congress of Anesthesiology.*
*Information:* Dr R. Mathias, Rua Caiubi 666, Sao Paulo, Brazil 05010.

**18–21 November.** Kyoto, Japan. *4th International Symposium on the Pain Clinic.*
*Information:* 4th WSPC Secretariat, Department of Anesthesiology, Osaka Medical College, c/o Inter Group Corp., Shohaku Bldg., 6–23 Chayamachi Kita-ku, Osaka 530, Japan.

**5–9 December.** San Juan. *15th Caribbean Symposium in Anaesthesia and Related Fields.*
*Information:* Miguel Colon-Morales, GPO Box 4547, San Juan, Puerto Rico 00936.

## 1991

**8–12 March.** San Antonio. *65th Congress of the International Anesthesia Research Society.*
*Information:* Emerson A. Moffitt, IARS, 3645 Warrensville Center Road, Cleveland, Ohio 44122, USA.

**9–12 May.** Washington DC. *6th International Dental Congress on Modern Pain Control.*
*Information:* American Dental Society of Anesthesiology, Inc., 211 E. Chicago Avenue, Suite 948, Chicago, IL 60611.

**21–25 June.** Quebec City. *48th Annual Meeting of Canadian Anaesthetists' Society.*
*Information:* Ms Ann Andrews, CAS, 187 Gerrard St. E., Toronto, Ontario M5A 2E5, Canada.

**26–30 October.** San Francisco. *American Society of Anesthesiologists Annual Meeting.*
*Information:* Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

### 1992

**29 March–2 April.** Atlanta, Georgia. *The Third International Symposium on the History of Anaesthesia.*
*Information:* R.K. Calverley, Medical Center, University of California, 225 Dickinson Street, San Diego, California CA 92103, 1990, USA.

**14–19 June.** The Hague. *10th World Congress of Anaesthesiology.*
*Information:* Dr Harm Lip, Nilantsweg, 99, 8041 AR Zwolle, Netherlands.

**17–21 October.** New Orleans. *American Society of Anesthesiologists Annual Meeting.*
*Information:* Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

### 1993

**15–17 September.** Edinburgh. *Joint Meeting with the Canadian Society of Anaesthetists.*
*Information:* The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

**9–13 October.** Washington DC. *American Society of Anesthesiologists Annual Meeting.*
*Information:* Executive Secretary, ASA 515 Busse Highway, Park Ridge, IL 60068, USA.

*Anaesthesia*, 1989, Volume 44, page 630

# Hazard Notice

**Air-Shields and Vickers Medical Syringe Pumps SP44 and SP55 (HC(Hazard)(89)8)**

These syringe pumps are susceptible to interference from electrostatic discharge. An appropriate modification can be made. Users should contact the manufacturers promptly to ensure that their pumps are modified.

# Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

*Dr J. N. Lunn, Editor of* ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

## PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (UK).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × $10\frac{1}{2}$ in. or $8\frac{1}{2}$ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author. *The manuscript* should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

*Number pages* consecutively, beginning with the title page.

## THE TITLE PAGE

*The name of the author and the address to which proofs and other correspondence are to be addressed* should appear in the top left-hand corner of the sheet.

*The main title* should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

*A subsidiary title* of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

*The names of the authors* should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. If there is more than one author the word 'AND' should be placed before the name of the last author.

*A line* should be typed across the title page below the author(s) name(s) in capitals.

*The author(s) name(s), degrees and designations* should be typed in lower case below the line. Initials should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

*A full postal institutional address* should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

## SUMMARY AND KEY WORDS

*Start a new sheet*

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

*Key (indexing) words.* Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

## COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

## THE TEXT

*Start a new sheet*

*The text of observational and experimental articles, case reports, etc.* is usually divided into sections with the headings *Introduction*, *Methods*, *Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

*Letters for the correspondence pages* should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

*Headings*: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.

(ii) Underlined words

These should be typed at the left-hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the sentence of the paragraph.

## ACKNOWLEDGMENTS

*Start a new sheet*

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

## REFERENCES

*Start a new sheet*

*Number references* consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble spaced typing.

Use the form of reference adopted by the US National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

*The titles of journals* should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscripts submitted but not yet accepted should be cited in the text as (unpublished observations) in parenthese.

The references must be verified by the author(s) against the original documents.

(*continued overleaf*)

*Examples of correct form of references*
*Note:* first and last pages in all references.

JOURNAL
*Standard journal article*—(List all authors)
Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

*Corporate author*
*The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology.* Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.
*Anonymous.* Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS
*Personal author(s)*
Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

*Corporate authors*
*American Medical Association Department of Drugs. AMA drug evaluations*, 3rd edn. New York: Publishing Sciences Group, 1977.

*Editor, compiler, chairman as author*
Rhodes AJ, Van Rooven CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

*Chapter in book*
Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: W.B. Saunders, 1974: 457–72.

*Agency publication*
*National Center for Health Statistics.* Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES
*Newspaper article*
Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

*Magazine article*
Roueche B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

## TABLES

*Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s)* should appear in the top right-hand corner.
*Indicate the approximate position* of each table in relation to the subject matter of the text in the left-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the left-hand margin of the text.

## FIGURES

*Each figure should be separate. Do not include figures in the text* but collect together in an envelope or folder.
*Indicate the approximate position* of each figure in relation to the subject matter of the text in the left-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.
All sources of identification of patients must be removed.

## LEGENDS FOR FIGURES

*Start a new sheet*
Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

## CONVENTIONS, ABBREVIATIONS AND STATISTICS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and $cmH_2O$. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).
The statistical tests used in the report should be stated clearly. Results should include 95% confidence limits for the main findings and probability estimates.

## LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be subject to considerable delay and may be returned to the author for revision.

***The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.***

## REVIEW JOURNALS

This journal is covered by *Current Contents, ASCA*, the *Science Citation Index and Index Medicus.*

# Seminars in Anesthesia

Editor:
RONALD L. KATZ

Editorial Board
**Richard J. Kitz, Emanuel M. Papper, John J. Bonica,**
**Werner Flacke and A.H. Giesecke, Jr.**

**Publication: Quarterly**
**Subscription: Volume 8, 1989**
**Institutions: £60.00 (UK)/$91.00 (Overseas)**

*Seminars in Anesthesia* will provide the anesthesiologist with a review of important topics in the field. Each issue will be devoted to an area of particular importance in which invited experts will discuss a wealth of clinical experience. All practising anesthesiologists will find *Seminars* a source of current and reliable information.

**From a recent issue**

Anesthesia for the Asthmatic Patient, *Ronald Dueck*
Thoracic Anesthesia, *Roger S. Wilson*
Anesthesia for Airway Surgery, *John V. Donlon, Jr*
Anesthesia for the Sickle Cell Diseases and Other Hemoglobinopathies, *Jeff Ray Gibson, Jr*
Anesthesia for Orthopedic Surgery, *Ralph L. Bernstein and Andrew D. Rosenberg*
Clinical Immunology of Chemonucleolysis, *Anna Uitvlugt and Jonathan Moss*
Clinical Aspects of Chemonucleolysis, *Joseph O. Reagan and Howard L. Zauder*
Anesthesia for Extracorporeal Shock Wave Lithotripsy, *David Gissen*

Coupon

**Seminars in Anesthesia**

*To: Journals Marketing Department*
*Academic Press Ltd*
*24–28 Oval Road*
*London NW1 7DX, England*

*Please tick*

☐ Please send me a sample copy and subscription details of *Seminars in Anesthesia*

Signature.......................................... Name (Capitals) ..........................................

Address ..........................................................................................................

.......................................................................................... Date..........................

# Contents: Anaesthesia, vol. 44, no. 7, July 1989

EDITORIAL
Neurophysiological monitoring
*P.F. Prior* 545

ORIGINAL ARTICLES
Anaphylaxis to latex during surgery
*F. Leynadier, C. Pecquet and J. Dry* 547
The pressor response and laryngeal mask insertion. A comparison with tracheal intubation
*N. Braude, E.A.F. Clements, U.M. Hodges and B.P. Andrews* 551
A double-blind comparison of epidural ketamine and diamorphine for postoperative analgesia
*S.J. Peat, P. Bras and M.H. Hanna* 555
Effect of single-dose omeprazole on intragastric acidity and volume during obstetric anaesthesia
*J. Moore, R.J. Flynn, M. Sampaio, C.M. Wilson and K.R.W. Gillon* 559
Gastric emptying after head injury
*I. Power, J.C. Easton, J.G. Todd and W.S. Nimmo* 563
Atracurium infusion during paediatric craniofacial surgery. Closed loop control of neuromuscular block
*C.M. Wait* and *V.A. Goat* 567
Postspinal headache in young and elderly patients. Two randomised, double-blind studies that compare 20- and 25-gauge needles
*B.S. Rasmussen, L. Blom, P. Hansen and S.S. Mikkelsen* 571
Migration of thoracic epidural catheters. Three methods for evaluation of catheter position in the thoracic epidural space
*J. Mourisse, M.J.M. Gielen, M.A.W.M. Hasenbos and F.M.J. Heystraten* 574
A comparison between open-end (single hole) and closed-end (three lateral holes) epidural catheters. Complications and quality of sensory blockade
*S. Michael, M.N. Richmond and R.J.S. Birks* 578
The requirement for intensive care support for the pregnant population
*S.G. Graham and M.C. Luxton* 581

CASE REPORTS
Recurrent anaphylactoid reaction during Caesarean section
*I.J.B. Jackson, M.R. Bryson, S. McPhail and B.B. Bhala* 585
Giant false aneurysm of the subclavian artery. An unusual complication of internal jugular venous cannulation
*S.P.J. Huddy, A. McEwan, J. Sabbat and D.J. Parker* 588

FORUM
Sodium bicarbonate as a single dose antacid in obstetric anaesthesia
*H.M.L. Mathews and J. Moore* 590
The effect of $H_2$ antagonists on duration of action of suxamethonium in the parturient
*D.G. Bogod and T.E. Oh* 591
Assessing collateral circulation in the hand—four methods compared
*R.J. Glavin and H.M. Jones* 594
Volatile agent use: perception and practice. A survey of agent use over a 3-year period
*J. Tarpey and P.G. Lawler* 596
Cardiovascular response during cerebral angiography under general and local anaesthesia
*D.G. Clayton, B.M. O'Donoghue, J.E. Stevens and P.E. Savage* 599
Reversal of prolonged sedation using flumazenil in critically ill patients
*A. Bodenham and G.R. Park* 603

SPECIAL ARTICLE
Anaesthesia and the law. Monitoring
*D. Brahams* 606

CORRESPONDENCE 608

BOOK REVIEWS 621

ANAESTHETIC LITERATURE 623

OBITUARIES 627

INTERNATIONAL CONGRESS CALENDAR 627

HAZARD NOTICE 630

Printed in Great Britain by The Whitefriars Press Ltd, member of BPCC Ltd, Tonbridge, Kent